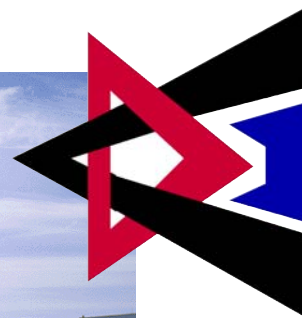


# **DEPARTMENT OF CLINICAL INVESTIGATION**

## **Annual Research Progress Report**

**Fiscal Year 2007**



**Madigan Army Medical Center  
Tacoma, Washington**



<b>REPORT DOCUMENTATION PAGE</b>				<i>Form Approved OMB No. 0704-0188</i>	
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**5d. PROJECT NUMBER.** Enter all project numbers as they appear in the report, e.g. 1F665702D1257; ILIR.

**5e. TASK NUMBER.** Enter all task numbers as they appear in the report, e.g. 05; RF0330201; T4112.

**5f. WORK UNIT NUMBER.** Enter all work unit numbers as they appear in the report, e.g. 001; AFAPL30480105.

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**ANNUAL PROGRESS REPORT**

30 SEPTEMBER 2007

DEPARTMENT OF CLINICAL INVESTIGATION

MADIGAN ARMY MEDICAL CENTER

TACOMA, WASHINGTON 98431

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**FISCAL YEAR 2007**  
**DEPARTMENT OF CLINICAL INVESTIGATION**  
**MADIGAN ARMY MEDICAL CENTER**  
**TACOMA, WASHINGTON 98431**

**Introduction**

In conducting the research described in this report, the investigators adhered to the “Guide for the Care and Use of Laboratory Animals” as prepared by the Committee on the Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Institutes of Health, and Title 9, Subchapter A, Parts I, II, and III of the Code of Federal Regulations. The investigators adhered to Title 21, Part 50 of the Code of Federal Regulations and the recommendations from the Declaration of Helsinki in the performance of investigations involving human subjects.

**Acknowledgments**

The DCI staff would like to acknowledge the significant and varied contributions of many individuals and organizations, all of whom were instrumental in making Madigan Army Medical Center (MAMC) research a resounding success in FY 2007. We appreciate the support and participation of the Western Regional Medical Center (WRMC) Command Leadership for fostering an environment where "Care with Compassion" is the motto and meticulous scientific process is the standard. We would like to thank our many corporate and industry research sponsors and partners, especially those foundations that foster military, medical research and support the Madigan community. We also would like to acknowledge the dedicated members of the Madigan Institutional Animal Care and Use Committee (IACUC), the Clinical Investigation Committee (CIC), and the Human Use Committee (HUC) whose tireless efforts ensured quality science and ethical conduct of our research. And, last but certainly not least, we would like to thank the hundreds of MAMC's military health care beneficiaries who volunteered to participate in so many demanding research studies, often when the only conceivable benefits were to individuals other than themselves.



## **Foreword**

### **Laboratory Animal Resources Service (LARS)**

There were 14 active animal use protocols during FY 2007, 9 were training and 5 were research oriented. Three additional protocols (one training and two research) either will restart or have been approved for start in FY 08. During this time our three military animal technicians positions were deleted and converted to civilian positions. The civilian positions will be filled in FY 08.

### **Research Administration Service (RAS)**

Formal research conducted in MAMC and the WRMC continues to be a solid and viable program. RAS processed 126 new protocols and oversaw 445 active protocols, about the same as in FY06. New initial and continuing review protocols continued to show 100% HIPAA compliance. New protocols reviewed at convened IRB meetings averaged around the same as in FY06 overall, but the numbers of expedited and exempt protocols increased slightly. There were no RAS personnel staffing changes during FY 07. The internal audit program continues to be well managed, and most protocols audited have shown satisfactory results. We will continue to include a few minimal risk retrospective review protocols in our audit program to ascertain whether the use of codes and the de-linking procedures described in the protocol are being adequately carried out. The RAS/Protocol Management Quality Improvement Team has continued to refine and implement improvements to local IRB administrative policies and procedures to include:

1. Updated entire SOP book in preparation for both DoD and FDA inspections, both of which occurred in June and September of 2007, respectively. Both showed no negative findings, although the FDA's was a verbal report. The FDA will send to DCI a final written report when it completes its final review.
2. Consolidated human use protocol template into one universal format for local and multicenter studies.
3. Developed an Exempt protocol template for research protocols where no link to PHI is indicated anywhere during the conduct of the study.
4. Coordinated 2 semi-annual Applied Research Training (ART) Courses, which are held in collaboration with the MAMC Faculty Development Fellows. Attendance averages about 50 students during the Fall and a little less in the Spring. Additionally, investigators still have the option of taking the required Human Subjects Research Protections training through DCI's subscription with the University of Miami's Collaborative IRB Training Initiative (CITI). Continuing Nursing and Medical education credits were added to the offerings.

Major FY08 plans include:

1. continually update the DCI website to offer more information and reporting options for investigators, to include updated templates to download;
2. continue to build up the constructive internal audit program;
3. participate in planning and speaking at the semi-annual ART Course and annual Madigan Research Day;
4. maintain close working relationship with the Foundations (Geneva, Jackson, and T.R.U.E.) to improve communication and assistance for the research program;
5. host and conduct the annual DCI HELPER Course for research coordinators working within MAMC.
6. adopt Lean Six Sigma quality improvement initiative of reducing approval times for research protocols and to reconfigure IRB committee.

## **Research Operations Service (ROS)**

The ROS continued to support a high level GME-related research activity this past year. The laboratory supported numerous basic research protocols within an active Maternal Fetal Medicine fellowship and submitted two March of Dimes grants based on collaborative efforts with the fellowship program. As of FY 2007, the lab supports 2 additional full-time research residents from the General Surgery department conducting research in stem cell biology and regenerative medicine. Translational research efforts continue through our clinical proteomics work using the SELDI-TOF mass spectrometry platform. The SELDI technology offers enormous potential for protein biomarker discovery in the analysis of clinical samples and application to other ongoing research projects. As the lab gains expertise in proteomic profiling, project work is being expanded to include pharmacoproteomic protocols and diagnosis of irritable bowel disease. The laboratory presented proteomics work at the 2006 annual Association of Medical Service Corps Officers of the Navy poster session held during the Association of Military Surgeons of the United States annual meeting and won the Best in Research Award. In addition to proteomics work, the lab is actively engaged in metagenomic profiling of clinical inflammatory bowel disease samples. In 2007, DCI enrolled 8 medical researchers in our annual Molecular Biology Short Course in support of our graduate medical education mission. The course offers a concrete research experience to Madigan residents and other novice medical researchers. Lab modules revolve around the processing and analysis of a clinical blood sample and include the genotyping of student DNA isolated from whole blood, culture and immunocytochemistry of mononuclear cell fractions, ELISA measurement, flow cytometry, and proteomic profiling of plasma. Lectures included more advanced applications of these techniques and literature review. The lab continues to develop a model neuromimetic cell culture system for neurobiology research through use of murine embryonic stem cells. Recent advances have addressed gene silencing issues in differentiated neurons opening up the possibility to develop several different cell-based assays of neural toxicity and the study of drug related signal transduction mechanisms. The lab is also conducting research on limb regeneration in newts by examining proteomic profiles of regenerating and non-regenerating limb tissue. Interns from our Bates Technical College internship program continue to make important contributions to lab productivity with the internship entering its third year. ROS anticipates a productive year in FY08 by sustaining growth and conducting research that promotes our educational mission and a spirit of collaboration between laboratory and medical center staff.

## UNIT SUMMARY - FISCAL YEAR 2007

### A. Objective:

Provide and create an environment to support clinical and basic medical research within Madigan Army Medical Center. Clinical Investigation exists to further the highest degree of medical readiness. DCI supports the Graduate Medical Education mission through leadership in curriculum development, medical education research, and military unique clinical investigations, as well as training opportunities available through institutional programs (ATLS, PALS, etc.)

### B. Technical Approach:

All research, investigational and training activities within the Department of Clinical Investigation are conducted under the guidance of the Office of Human Research Protections (OHRP), Food & Drug Administration (FDA), AR 40-7, AR 40-38, AR 70-25, and AR 40-33. Careful monitoring of all approved protocols is conducted in order to assure strict compliance with the applicable regulations.

### C. Staffing:

Name	Rank	MOS	Title
Amoroso, Paul	COL	61N	Chief, DCI
° McCune, David	LTC	61B	Chief, Clinical Studies Svc
– Arroyo-Ortiz, Lissette	GS11	0671	Administrative Officer
Patience, Troy	GS11	1530	Statistician (Medicine)
Atoigue, Lucy	GS06	0318	Secretary/Steno
Porreca, Mary	GS05	0303	Research Protocol Clerk
Merrill, Nancy	MAJ	64C	Chief, Lab Animal Res Svc
– Van Loon, Karen	SFC	91T	Animal Technologist & NCOIC
Teadt, Anita	SGT	91T	Animal Technologist
– Phyll, Shayla	SPC	91T	Animal Technologist
– Phillips, Miemie	SPC	91T	Animal Technologist
Theis, Jennifer	GS11	0301	Trauma Training Specialist
Spahn-Bridges, Shelley	WG05	5048	Animal Caretaker
Hartenstine, Micheal	CPT	71B	Molecular Biologist
Wright, James	GS11	0644	Medical Technologist
Bullock, Jeff	GS11	0644	Medical Technologist
DeHart, Mary	GS11	0644	Medical Technologist
Ippolito, Dannielle	GS11	0644	Medical Technologist
– Cederholm, Heidi	GS11	0644	Medical Technologist
Bergmann, Aspen	GS11	0644	Medical Technologist
Lai, Lonnie	GS13	0610	Chief, Research Admin Svc
Jones, Barbara	GS11	0301	Auditor
Rayner, Athena	GS09	0303	Research Protocol Specialist
Lund, Jill	GS07	0303	Research Protocol Assistant

#### Staff Additions & Departures

##### Departures

Arroyo-Ortiz, Sep 2007	Phyll, Nov 2006
Van Loon, Jun 2007	Cederholm, Jul 2007
Phillips, Sep 2007	

**Staffing Summary:**

<u>Personnel:</u>	<u>Authorized</u>	<u>Required</u>	<u>Assigned</u>
Officers	4	4	4
Civilians	19	21	14
Enlisted	2	2	1

**D. Funding:**

P8 Funds.	\$2,224,041
Civilian Pay:	\$1,157,439
Contracts:	\$24,101
Consumable Supplies:	\$109,290
CEEP Equipments:	\$276,527
Travel:	\$11,362
Print/Publications:	\$-
MEDCASE:	\$100,660
Military Pay:	\$544,662
CRADA:	\$244,058
Federal Grants.	\$267,921
USAMRMC:	\$50,000
NCI:	\$137,550
Triservice Nursing:	\$63,817
Other (DWHRP, etc.):	\$16,554

## **E. Progress**

During FY 2007, there were 445 active protocols that received administrative and/or technical support during the year, of these, 280 are presently ongoing, 111 were completed, 52 were terminated, and 2 animal protocols reached their 3 year anniversary and expired. The principal investigator distribution was as follows: 334 staff protocols, 93 resident protocols, 12 fellow protocols, 4 intern protocols, and 2 Special Forces Group protocols. There were 126 new protocols.

There were 91 publications in publicly available sources and 188 presentations at regional or national medical association meetings.

## **F. Program Support**

**Programs supported by DCI:** 10 internships, 15 residencies, 5 fellowships, and 7 non-MC programs; they are:

*Internships:* Emergency Medicine, Family Practice, General Surgery, Internal Medicine, Neurology, Obstetrics and Gynecology, Orthopaedic Surgery, Pathology, Pediatrics, and Transitional Year.

*Residencies:* Emergency Medicine, Family Practice, General Surgery, Internal Medicine, Neurology, Obstetrics and Gynecology, Ophthalmology, Oral and Maxillofacial Surgery, Orthopaedic Surgery, Otolaryngology, Pathology, Pediatrics, Preventive Medicine (Public Health), Radiology (Diagnostic), and Urology.

*Fellowships:* Developmental Pediatrics, Faculty Development (Family Practice), Geriatric Medicine, Maternal-Fetal Medicine, and Urogynecology.

*Non-MC programs:* Diabetic Foot Fellowship, Occupational Therapy, Pediatric Psychology, Pharmacy Practice, Physician Assistant Program (Emergency Medicine & Orthopaedics), and Podiatry.

### **Other training protocols supported by DCI:**

DCI: 203023

Department of Surgery: 205017, 205079, 206006, 206030, 206078

Department of Obstetrics & Gynecology: 206029

Department of Pediatrics: 204028, 207025, 207044

Department of Nursing: 207015

Special Forces: 206018, 206106

## **G. Committee Members**

### Clinical Investigation Committee

COL Paul Amoroso, MC  
Chairman

Chief or delegated representative of:

Department of Anesthesia and Operative Services  
Department of Emergency Medicine  
Department of Family Practice  
Department of Medicine  
Department of Nursing  
Department of OB/GYN  
Department of Pathology  
Department of Pediatrics  
Department of Preventive Medicine  
Department of Radiology  
Department of Surgery  
Pharmacy Service  
Physical Medicine & Rehabilitation Service  
Department of Clinical Investigation (DCI)  
Clinical Studies Service, DCI  
Medical Statistician, DCI  
Research Administration Service, DCI  
Research Operations Service, DCI  
General Surgery Research Resident, DCI

Human Use Committee  
COL Paul J. Amoroso, MC  
Chairman

Chief or delegated representative of:

- Department of Nursing
- Department of Pediatrics
- Department of Radiology
- Department of Ministry and Pastoral Care
- Department of Clinical Investigation
- Research Administration Service, DCI
- Pharmacy Service
- Social Work Service
- Center Judge Advocate
- Non-institutional Member

Institutional Animal Care & Use Committee  
LTC Andrew C. Peterson, MC  
Chairman

Chief or delegated representative of:

- Department of Clinical Investigation (DCI)
- Department of Pathology
- Department of Medicine
- Department of Surgery
- Anderson Simulation Center
- Special Forces Veterinarian
- Non-affiliated Member and Alternate Non-affiliated Member
- Attending Veterinarian, DCI
- Animal Care Worker, DCI

## H. Awards

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### Manuscript Awards

#### **MG Byron L. Steger Research Award**

This award is given to a resident, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research

**Presented to:** CPT Matthew Eckert, MC; General Surgery Service, Department of Surgery for his paper entitled: "Bronchoscopy in the Blast Injury Patient"

#### **COL Patrick S. Madigan Foundation Research Award**

This award is given to a fellow, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

**Presented to:** CDR Richard Samms, MC; Department of Family Medicine for his paper entitled: "Developing a Family Medicine Residency Medical Ethics Curriculum: Introducing a New Learning Needs Assessment Tool"

#### **MG Kenyon Joyce Research Award**

This award is given to staff, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

**Presented to:** COL Peter E. Nielsen, MC; Department of Obstetrics/Gynecology for his paper entitled: "Effects of teamwork Training on Adverse Outcomes and Process of Care in Labor and Delivery"

---

### Madigan Research Day Presentation Awards

These awards are given after the annual Madigan Research Day to recognize the best presentation in each of the 5 oral presentation sessions and the poster session. This year's winners are:

#### **Case Report Session**

**Presented to:** Kristine Kalbfleisch, MD, MS; Department of Emergency Medicine

#### **Experimental Design Session**

**Presented to:** CPT Lynne Kramer, MC; Department of Pediatrics

#### **Managed Care and Outcomes Session**

**Presented to:** CPT Ryan Lehmann, MC; General Surgery Service, Department of Surgery



## **Medical Education Research Session**

**Presented to:** MAJ Shad Deering, MC; Department of Obstetrics/Gynecology & Charles A. Andersen Simulation Center

## **Military Unique Clinical Investigation Session**

**Presented to:** CPT Kristin Erickson, MC; Department of Preventive Medicine

## **Poster Session**

**Presented to:** CPT April Fritch, MS; Behavioral Health; Department of Psychology

---

## **Madigan Research Day Special Awards**

### ***BG GEORGE J. BROWN MENTOR'S CUBE***

The BG George J. Brown Mentor's Cube honors the vital role of the mentor in the process of medical education and research. Madigan Research Day celebrates the breadth and depth of scholarly activity performed at MAMC. The BG George J. Brown Mentor's Cube honors this vital core attribute of excellence in medical scholarship.

**Presented to:** COL Mary P. Fairchok, MC; Department of Pediatrics

### ***NANCY J. WHITTEN OUTSTANDING IRB MEMBER AWARD***

This award was created to recognize a member of our Institutional Review Board who has gone beyond the normal excellent service.

**Presented to:** MAJ William Kelly, MC; Pulmonary Disease/Critical Care Service, Department of Medicine

### ***BG MACK C. HILL FACILITATOR'S AWARD***

This award was created to recognize a Madigan member who has helped to facilitate the center's research mission in ways that are not always apparent to the general population. This individual represents the epitome of selfless service through their continual and frequent transparent support of others success .... they exhibit a generous customer service attitude.

**Presented to:** MAJ Joseph Topinka, JA; Center Judge Advocate Office

### ***BG MICHAEL R. DUNN 'PRESS-ON' ENERGY AWARD***

The award is an obelisk which signifies the interconnecting spheres of the physical, mental and spiritual in the human experience. The BG Michael A. Dunn Award recognizes that the attributes of persistence and determination are at least as, and perhaps, more important than talent, genius or education in reaching meaningful goals.

**Presented to:** Athena Rayner, BS; Department of Clinical Investigation

### ***CHARLES A. ANDERSEN AWARD FOR SIMULATION RESEARCH***

This award was created to encourage and recognize outstanding research in the field of Medical Simulation at Madigan Army Medical Center as it relates to improving training, performance, new educational techniques, or patient safety issues.

**Presented to:** Kristina Stillsnoking; Charles A. Anderson Simulation Center

## **I. Presentations**

### **Department of Anesthesia & Operative Services**

Holt HE. Challenges of Managing Chronic Pain in a Multidisciplinary Military Medical Center. Presented at WANA Conference, Seattle, WA, April 2007.

Miller JP. TEE Review Course III: Putting It All Together, The Aortic Valve. Presented at Society of Cardiovascular Anesthesiologists Annual Meeting, Montreal, Canada, April 2007.

Wander GD, Ellis J, Spanton J. The Effect of a Single Dose of Kava and Midazolam on Emergence Time from General Anesthesia Following an Abdominal Surgical Procedure in the Male Sprague-Dawley Rat. Presented at Annual Meeting, Washing Association of Nurse Anesthetists, SeaTac, WA, April 2007.

### **Department of Clinical Investigation**

Amoroso PJ. Service Status and Related Factors Influencing Millennium Cohort Enrollment and Retention. Presented at 8th Annual Meeting of the Scientific Steering and Advisory Committee, San Diego, CA, April 2007.

Celver JP, Cederholm HM, Hartenstine MJ, McNutt PM. Murine embryonic stemcell (mESC) derived neurons as a renewable culture system for botulinum neurotoxin research. Presented at Association of Medical Service Corps Officers of the Navy/Anscom), San Antonio, TX, November 2006.

Celver JP, Gotkin JL, Napolitano PG, Hill DL, McNutt PM. Specific Inhibition of ERK1/2 activation by progesterone blocks LPS induced IL-6 secretion in fetal and maternal mononuclear cells. Presented at Society for Maternal Fetal Medicine, San Francisco, CA, February 2007.

Hartenstine MJ, Ippolito DL, Cederholm HM, Bergmann AM, Napolitano PG, McNutt PM. Longitudinal Proteomic Analysis of Lower Abundance Plasma Proteins by SELDI-TOF Profiling and Antibody Microarray. Presented at 27th Annual Meeting of the Society for Maternal Fetal Medicine, San Francisco, CA, February 2007.

Hartenstine MJ, Ippolito DL, Herbert GS, Eckert MJ, Cederholm HM, Bergmann AM, Napolitano PG, Celver JP, McNutt PM. Proteomic Profiling of Maternal Plasma Collected Longitudinally during Pregnancy by SELDI-TOF MS and Antibody Microarray. Presented at 14th Annual AMSCON Poster Session, San Antonio, TX, November 2006.

Ippolito DL, Hartenstine MJ, Cederholm HM, Bergmann AM, Napolitano P, Celver JP, McNutt PM. Proteomic profiling of maternal plasma collected longitudinally during pregnancy by surface-enhanced laser desorption time of flight mass spectrometry (SELDI-TOF MS). Presented at Society for Maternal Fetal Medicine, San Francisco, CA, February 2007.

Ippolito DL, Hartenstine MJ, Celver JP, Cederholm HM, Bergmann AM, Napolitano PG, McNutt PM. Longitudinal Proteomic Profiling of Maternal Plasma by SELDITOF MS. Presented at HUPO 2007, Seattle, WA, March 2007.

Jacobson IG, Ryan M, Smith TC, Bell NS, Amoroso PJ, Hooper TI, Wells TS, Boyko EJ, Gackstetter GG. How did Deployment is Support of the Global War on Terrorism Impact Alcohol Use and Alcohol Related Problems in a Large Military Cohort. Presented at NEHC 46th Navy Occupational Health and Preventive Medicine Conference, Hampton, VA, March 2007.

Jacobson IG, Smith TC, Smith B, Amoroso PJ, Wells TS, Bathalon GP, Keel PK, Ryan M. Disordered Eating and Weight Changes after Deployment in Support of the Global War on Terrorism. Presented at Naval Environmental Health Center, Hampton, VA, March 2007.

Sulsky SI, Parsons W, Grabenstein JD, Ford SM, Amoroso PJ, Maynard C, Boyko E. Disability discharge among United States Army Personnel vaccinated against anthrax (1998-2005). Presented at 10th Annual Force Health Protection Conference, Louisville, KY, August 2007.

Sulsky SS, Amoroso PJ, Wallace RF, Schwartz CE, Hill OT. Effective use of administrative data for evaluation research: The Parachute Ankle Brace. Presented at 10th Annual Force Health Protection, Louisville, KY, August 2007.

## **Department of Emergency Medicine**

Blankenship RB. Advanced Uses of Palm-Based Handhelds. Presented at Scientific Assembly, New Orleans, LA, October 2006.

Blankenship RB. Electronic Emergency Department Record: Do the Write Thing. Presented at Scientific Assembly, New Orleans, LA, October 2006.

Blankenship RB. Emergency Medicine on the Front Lines: Lessons in Leadership. Presented at EMRA's Plenary Session - Scientific Assembly, New Orleans, LA, October 2006.

Blankenship RB. Handholding for Handhelds: Palmtop Principles for the Practitioner. Presented at Scientific Assembly, New Orleans, LA, October 2006.

Blankenship RB, Harrison. Potential Benefit of Web-based Instruction or Simulation Training Over Traditional Didactic Pelvic Ultrasound Lectures. Presented at CORD Annual Meeting 2006, Las Vegas, 2006.

Givens ML, Culica D. Characterization of Computer Algorithm Classified Emergency Department Visits. Presented at Research Forum, ACEP Scientific Assembly, New Orleans, LA, October 2006.

Givens ML, Kalbfleisch K, Bryson S. Inhalation of Methanol Containing Products - A Significant Source of Toxicity. Presented at Research Forum, ACEP Scientific Assembly, New Orleans, LA, October 2006.

## **Department of Family Medicine**

Domagalski JE. Genital Co-Infection with Herpes Simplex Viruses Type 1 and 2: Testing and Diagnosis Issues. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Kimmer SL. Pediatric Obesity in a Military Family Medicine Clinic. Presented at US Academy of Family Physicians Annual meeting, Hilton Head, SC, March 2007.

Maurer DM. Life as an Army Physician. Presented at Recruiting Doctors in Eastern Washington, Spokane, WA, February 2007.

Poffenberger NA. Impact of Case Management of Care of At-risk Patients Taking High Dose Opioid Medications. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Rosen IM. Determinants of Medical Student Interest in Family Medicine. Presented at STFM, Chicago, IL, April 2007.

Runser L, Short M, Kelly K. Gastrointestinal Endoscopy by a Family Physician: A Case Series Demonstrating Healthcare Savings. Presented at 2007 Annual Meeting and Exposition, Hilton Head, SC, March 2007.

Sigmon MJ. Where There's Smoke, Is there Disease? A Study of Environmental Airborne Exposures in Soldier Returning from Iraq. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Sigmon MJ, Cook JE. Where there's smoke, is there disease? Presented at University of Washington, Seattle, WA, May 2007.

Smoley BA, Smith N, Runkle GP, Edwards JA. Prevalence of Hypertension in a Population of Active Duty Service Members. Presented at 2007 USAFP Annual Meeting, Hilton Head, SC, March 2007.

Swenson CN. Collaborative Practice to Manage Chronic Nonmalignant Pain (CNP) Tools and Tips. Presented at American Society of Health System, Anaheim, CA, December 2006.

## **Health Outcomes Management Division**

Whitaker RP, Birgenheier PS, Hunt AH, Meyer JG. Transformation of Military Case Management and Medical Holdover Operations. Presented at Case Management Society of America, Denver, CO, June 2007.

## **Infectious Disease Service, Department of Medicine**

Ake JA, Coyle JR, Wojciehowski AO, Morris JT. Risk Behavior, Knowledge, and Attitudes of ROTC Cadets Regarding HIV/AIDS. Presented at Infectious Diseases Society of America, 44th Annual Meeting, Toronto, Canada, October 2006.

## **Internal Medicine Service, Department of Medicine**

Ake JA. Pcp IN a patient with dermatomyositis complicated by usual interstitial pneumonitis: are current PCP prophylaxis strategies appropriate? Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2006.

Allison JC. Medical Care in Iraq: One Military Physician's Experience. Presented at Brihan Maharashtra Mandal Medical Conference, Seattle, WA, June 2007.

Avalos C. Methotrexate induced pneumonitis. Presented at Army American College of Physician Annual Meeting, November 2006.

Bauler KC. A patient with progressive dyspnea: the impact of altitude on chronic pulmonary disease. Presented at Army American College of Physicians Annual Meeting, November 2006.

Broy CC. Gitelman's Disease in a Patient with Nephrocalcinosis Secondary to Hyperparathyroidism. Presented at Army American College of Physicians Annual Meeting, November 2006.

Coyle JR. Empiric Therapy in FUO: A Case Report and Literature Review. Presented at Army American College of Physicians Annual Meeting, November 2006.

DeHaan PJ. A case of disappearing platelets. Presented at Army American College of Physicians Annual Meeting, November 2006.

Evans NR. Recurrent syncope and prolonged QT interval in a patient taking Methadone. Presented at Army American College of Physicians Annual Meeting, November 2006.

Ferguson JW. Successful treatment of refractory thrombotic thrombocytopenic purpura with Cyclosporine. Presented at Army American College of Physicians Annual Meeting, November 2006.

Krier MJ. How idiopathic is idiopathic pulmonary fibrosis - A case of vertical banding gastropasty, abnormal reflux and now lung transplant. Presented at Army American College of Physicians Annual Meeting, November 2006.

Kwon HP. Hemoptysis in the young and indications for bronchoscopy. Presented at Army American College of Physicians Annual Meeting, November 2006.

Kwon HP, Simonson KA, Niven AS, Mysliwiec V. Hemoptysis in Young Adults. Presented at American College of Physicians Internal Medicine 2007, San Diego, CA, April 2007.

Olagesthin SA. A PET positive lingular lung mass in a patient on Amiodarone. Presented at Army American College of Physicians Annual Meeting, November 2006.

Powell DF. Progressive pulmonary infiltrates and bronchiectasis in a patient with T-cell lymphoma. Presented at Army American College of Physicians Annual Meeting, November 2006.

Powell DF. Stereotactic radiosurgery improves pre-treatment symptoms in patient with acoustic neuroma. Presented at Army American College of Physicians Annual Meeting, November 2006.

Reilly SC. Improving patient outcomes using a collaborative cardiovascular pharmacotherapy (CCP) clinic. Presented at Army American College of Physicians Annual Meeting, November 2006.

Sapp JE. Oxygen toxicity during a tactical dive on closed-circuit oxygen. Presented at Army American College of Physicians Annual Meeting, November 2006.

Sapp JE, Mysliwiec V, Niven AS. Effect of Fluticasone/Salmeterol, Tiotropium, or Bothe on FEV<sub>1</sub> and Healthcare Utilization in Patients With Chronic Obstructive Pulmonary Disease (COPD). Presented at A/AF American College of Physicians Annual Session, San Antonio, TX, USA, November 2007.

Shelhamer MC. An unusual presentation of acute tubular necrosis manifesting as a nephrosis. Presented at Army American College of Physicians Annual Meeting, November 2006.

Smith ME. Eosinophilic esophagitis. Presented at Army American College of Physicians Annual Meeting, November 2006.

Uy AL. Severe pulmonary coccidiomycosis infection in a National Guard infantryman. Presented at Army American College of Physicians Annual Meeting, November 2006.

Venkataraman RG. Nonoperative treatment of cervical osteomyelitis associated with epidural abscess and nerve root compression. Presented at Army American College of Physicians Annual Meeting, November 2006.

Williamson NA. A re-emerging infection? Presented at Army American College of Physicians Annual Meeting, November 2006.

Wilton NK. Successful treatment of autologous saphenous vein graft with antibiotics alone. Presented at Army American College of Physicians Annual Meeting, November 2006.

## **Neurology Service, Department of Medicine**

Kozminski MP. A Case of Miller Fisher Syndrome. Presented at Washington State Neurological Society, WA, October 2006.

Langford DR. Patient Knowledge and Expectations of EMG-NCS Prior to Procedure. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Langford DR, Erickson JC, Theeler BJ, Scott BR, McDonald JM. Rapid Improvement of Paraneoplastic Cerebellar Degeneration after Thymectomy in a Patient with Occult Ovarian Cancer. Presented at American Academy of Neurology, 59th Annual Meeting, Boston, MA, May 2007.

Lee JD, Erickson JC. Evaluating Acute Altered Mental Status: Are Incoming Interns Prepared? Presented at American Academy of Neurology 59th Annual Meeting, Boston, MA, May 2007.

Theeler BJ. A case of Isolated Intracranial Rosai-Dorfman Disease Presenting as a Meningioma: Clinical Radiologic and Pathologic Characteristics. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Theeler BJ. Prevalence and Impact of Migraine Among U.S. Army Soldiers Deployed to Iraq. Presented at Washington State Neurological Society, WA, October 2006.

Theeler BJ, Erickson JC. Clinical Characteristics of Post-Traumatic Headache in U.S. Army Soldiers Deployed to Iraq. Presented at American Academy of Pain Management, Las Vegas, NV, September 2007.

## **Pulmonary Disease & Critical Care Service, Department of Medicine**

Niven A. Critical Care in Iraq: Lessons From the Combat Support Hospital. Presented at Lung Day 2007, UW Pulmonary/Critical Care Division, Seattle, WA, June 2007.

## **Department of Nursing**

Carlsson GE, McCann SA, Raymundo EA. Investigation of Modulation of the Alpha 2 Receptor in Corydalis Analgesia. Presented at Perinatal Care Conference, SeaTac, WA, April 2007.

Darnell JN, Loan LA. Military Readiness Risks: Military Leader Experiences with Mandatory Addiction Referrals. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Feider LL, Mitchell PH, Bridges E, Gallucci BJ, Loan LA. Oral Care Practice Survey for the Orally Intubated Adult Critically Ill Patient. Presented at Perinatal Care Conference, Portland, OR, April 2007.

Feider LL, Mitchell PH, Bridges E, Gallucci BJ, Loan LA. Survey Development Reliability & Validity Measures of Oral Care Practices for the Orally Intubated Adult Critically Ill Patient. Presented at Perinatal Care Conference, Honolulu, HI, March 2007.

Feider LL, Mitchell PH, Bridges E, Gallucci BJ, Loan LA. Survey of Oral Care Practices for the Orally Intubated Adult Critically Ill Patient. Presented at Perinatal Care Conference, Honolulu, HI, March 2007.

Garner BK, Wilkie DJ. Validity & Reliability of Checklist for Nonverbal Pain Indicators in Patients with Lung Cancer. Presented at Perinatal Care Conference, Honolulu, HI, March 2007.

Hopkins-Chadwick DL. Army Nurse Corps Officers Reintegration Experiences after a Deployment to Operations Enduring Freedom or Iraqi Freedom. Presented at Perinatal Care Conference, Ft. Lewis, WA, April 2007.

Hopkins-Chadwick DL. Women, Work and Health: The Case for Resilience. Presented at Perinatal Care Conference, Washington, DC, October 2006.

Loan LA. From Numbers to Knowledge to Know How: Using Military Nursing Outcomes Database Data to Decrease Patient Falls & Medication Errors. Presented at Perinatal Care Conference, Washington, DC, January 2007.

Loan LA, McCarthy MS. Using Military Nursing Outcomes Database Pressure Ulcer Prevalence Data to Improve Patient & Cost Outcomes. Presented at Perinatal Care Conference, Washington, DC, January 2007.

Loan LA, McCarthy MS, Raymond SM, Mendoza D, Patrician PA, Brosch LR. From Numbers to Knowledge to Know-How: Using Military Nursing Outcomes Database (MilNOD) Pressure Ulcer Prevalence Data to Improve Patient and Cost Outcomes. Presented at Perinatal Care Conference, San Antonio, TX, November 2006.

Loan LA, Whitney D, Taylor JA, Blackburn S. The Impact of Inpatient Computer Physician Order Entry on Medication Administration Variance Rates in Neonatal Intermediate and Intensive Care Units. Presented at Perinatal Care Conference, San Antonio, TX, November 2006.

McCarthy MS. Wound Healing in the Critical Care Setting. Presented at Perinatal Care Conference, Phoenix, AZ, January 2007.

McCarthy MS, Sorensen DM, Elshaw EB, Simonson KA, Baumgartner BJ, Demars SM. Perioperative Immunonutrition in Head and Neck Cancer: A Pilot Study. Presented at Perinatal Care Conference, Phoenix, AZ, January 2007.

McNabb LA, Hopkins-Chadwick DL, Loan LA, McCarthy MS. ANC Retention Study Brief. Presented at Perinatal Care Conference, April 2007.

Priester MD. Advances in Battlefield Care From Vietnam to Operation Iraqi Freedom. Presented at Perinatal Care Conference, Tukwila, WA, September 2007.

Ramsdell MJ, Berry DL. Evaluating cognitive dysfunction in women newly diagnosed with breast cancer receiving chemotherapy. Presented at Perinatal Care Conference, Seattle, WA, January 2007.

Reyes S, Stillsmoking K, Deering S, Hopkins-Chadwick D. Implementation & Evaluation of the Virtual IV Simulator in Teaching Intravenous Initiation Skills to 91WM6 Practical Nurse Course Students. Presented at Perinatal Care Conference, Honolulu, HI, March 2007.

Stillsmoking K. Implementation and Evaluation of the Addition of a Virtual Reality System in Teaching Intravenous Initiation Skills to 91WM6 Practical Nurse Course Students. Presented at Perinatal Care Conference, Ft. Lewis, WA, April 2007.

Stillsmoking K, Reyes S, Deering S. Implementation & Evaluation of the Addition of a Virtual Reality System in Teaching Intravenous Initiation Skills to 91WM6 Practical Nurse Course Students. Presented at Perinatal Care Conference, Orlando, FL, January 2007.

Tebbs JS, Hopkins-Chadwick DL. Decreasing Behavioral Restraint Use: A Workload Management Approach. Presented at Perinatal Care Conference, San Antonio, TX, November 2006.

Tebbs JS, Hopkins-Chadwick DL. Decreasing Behavioral Restraint Use: A Workload Management Approach. Presented at Perinatal Care Conference, Honolulu, HI, March 2007.

Trego LL. Menstruation During Deployment: Attitudes Towards Menstrual Suppression. Presented at Perinatal Care Conference, Portland, OR, April 2007.

Trego LL. Menstruation During Deployment: Attitudes Towards Menstrual Suppression. Presented at Perinatal Care Conference, Ft Lewis, WA, April 2007.

Wheat LL, Eichelberger CL, Laver TE, Hacker JB. The Effects of Chrysin, A Passiflora Incarnata Extract and Midazolam on Emergence Time from anesthesia in Male Sprague-Dawley Rats after Intra-Abdominal Surgery. Presented at Perinatal Care Conference, SeaTac, WA, April 2007.

## **Department of Obstetrics/Gynecology**

Deering SH. Validation and testing of a postpartum hemorrhage simulator for instruction and evaluation of residents. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Gotkin JL, Howard B, Deering S, Cerver J, Napolitano P, McNutt P, Hill D. Response of isolated monocytes and lymphocytes to LPS and progesterone. Presented at Society for Maternal Fetal Medicine, San Francisco, CA, February 2007.

Han J, Fowers R, Parker J, Hibbert M, Nielson P, Dainty L. Efficacy of Misoprostol for Non-viable First Trimester Pregnancy: A Comparison of Medical and Expectant Management. Presented at Armed Forces District Meeting, Sonthofen, Germany, October 2006.

Hill D. Progesterone receptor Isoform C is expressed in fetal and maternal mononuclear cells. Presented at Society of Maternal Fetal Medicine, San Francisco, CA, February 2007.

Lattu A. The distribution and predictive value of Bishop scores in nulliparas between 37-42 weeks gestation. Presented at 2007 American College of Obstetrics (ACOG), San Diego, CA, May 2007.

Lattu AL. The Distribution and Predictive Value of Bishop Scores in Nulliparas Between 37-42 Weeks Gestation. Presented at 2007 American College of Obstetrics and Gynecology Annual Clinical Meeting, San Diego, CA, May 2007.

Lattu AL. Use of pipelle endometrial sampling in the evaluation of abnormal first trimester pregnancy. Presented at ACOG Armed Forces District Meeting, Sonthofen, Germany, October 2006.

Murphy CS. Women's Healthcare in OPERATION IRAQI FREEDOM: A Survey of Camps with Echelon Three Facilities. Presented at 2006 AFD Annual Meeting, Sonthofen, Germany, October 2006.

Nielsen PE. Leadership Services to the Nation and Our Patients. Presented at Beth Israel Deaconess Medical Center, Boston, MA, May 2007.

Vaccaro CM, Clemons JL. Correlation of Persistent Anal Sphincter Defects & Symptoms Following Primary Repair of Obstetric Anal Sphincter Lacerations. Presented at AUGS, Hollywood, FL, September 2007.

Zalucki C, Clemons J. Correlation of Persistent Anal Sphincter Defects and Symptoms Following Repair of Anal Sphincter Lacerations in Primiparous Women. Presented at Armed Forces District Meeting, Global Partnership for Women's Health, Sonthofen, Germany, October 2006.

## **Department of Pathology**

Chong H. Use of MS2 E. Coli Bacteriophage for RNA Virus Extraction Control. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

O'Brien KL, Champeaux AL. The Laboratory Officer on Duty as a Member of the Trauma Team. Presented at American Association of Blood Banks 2006 National Meeting, Miami, Florida, October 2006.

Perkins D. Romanian "Lily Pads": Force Health Protection Issues. Presented at USACHPPM 10th Annual Conference Force Health Protection, Louisville, KY, August 2007.

Perkins DS. Determining Mupirocin Resistance in Clinical Isolates of Methicillin resistant Staphylococcus aureus. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

## **Department of Pediatrics**

Bondi SA. Iron-deficiency Anemia in Toddlers Due to Excessive Cow's Milk Ingestion - Two Unusual Presentations. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Cartwright VW, Devenport MJ, Puntel RA. Screening EKGs in ROTC Cadets. Presented at Uniformed Services Pediatric Seminar, American Academy of Pediatrics, Spring 2007.

Cartwright VW, Heifert T. Autoimmune Hepatitis and Juvenile Arthritis: A Unique Combination. Presented at Uniformed Services Pediatric Seminar, American Academy of Pediatrics, Spring 2007.

Cartwright VW, Rowe C, Puntel R. Infant Lumbar Puncture Simulation is Valuable for Pediatric Resident Training. Presented at Uniformed Services Pediatric Seminar, American Academy of Pediatrics, Spring 2007.

Dramer LC. Alternating Antipyretics: Antipyretic Efficacy of Acetaminophen versus Acetaminophen Alternated with Ibuprofen in Children. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.



Ervin MK, Davis BE, Kelly PC. Correlates of Bone Mineral Density in Adolescent Girls with Neuromuscular Disabilities: A Pilot Study. Presented at Pediatric Academic Societies Meeting, Toronto, Canada, May 2007.

Estroff DT. Immunization Update - new vaccines and schedules. Presented at Pierce County Medical Society Public - School Health Committee, WA, November 2006.

Flake EM. Early Literacy Promotion in a Military Pediatric Clinic. Presented at 10th Annual Madigan Research Day, Ft. Lewis, WA, April 2007.

Giamanco NM. Severe Pseudotumor Cerebri Associated With Minocycline in an Adolescent Female. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Heifert TA. Juvenile Idiopathic Arthritis Presenting Years after onset of Autoimmune Hepatitis. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Hogue JS, Fairchok MP, Perkins DS, Viscount HB. Mupirocin Resistance in Clinical Isolates of Methicillin-Resistant Staphylococcus aureus in a Primary Care Population. Presented at Infectious Disease Society of America Annual Meeting, San Diego, CA, October 2007.

Kramer LC, Thompson A, Richards P, Harper D, Fairchok M. Alternating antipyretics: Antipyretic efficacy of acetaminophen versus acetaminophen alternated with ibuprofen in children. Presented at Uniformed Services Pediatric Seminar, Bethesda, MD, March 2007.

Limjuco JR. Utilizing CSF PCR to reveal unsuspected Varicella-Zoster meningitis. Presented at Uniformed Services Pediatric Seminar (USPS), Bethesda, MD, March 2007.

Limjuco JR. Utilizing CSF PCR to reveal unsuspected Varicella-Zoster Meningitis. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Maranich AM, Mahlen SD, Chong HY, Fairchok MP. The Panton Valentine Leucocidin Virulence Factor in Staphylococcus aureus Disease. Presented at Infectious Disease Society of America, Toronto, Canada, October 2006.

Puntel RA. EKG Screening in ROTC Cadets: Is it Useful? Presented at Madigan Research Day, Ft Lewis, WA, April 2007.

## **Department of Pharmacy**

Dydek GJ, Tomich DJ. Development of a peer review process for provision of pharmacy medication management services. Presented at American Society of Health-System Pharmacists, 41st ASHP Midyear Clinical Mtg, Anaheim, CA, December 2006.

Hudak ME. Consequences of Triple Therapy: Evaluation of Bleeding and Embolic Events in a Cohort of Patients Taking Aspirin, Clopidogrel and Warfarin Concomitantly. Presented at Northwest Pharmacy Seminar, Coeur'd Lene, Idaho, June 2007.

Swenson CN, Hudak ME. Evaluation of Bleeding and Thromboembolic Events in a Cohort of Stented and Non-Stented Patients Taking Aspirin, Clopidogrel and Warfarin Concomitantly. Presented at Western States Residency Conference, Pacific Grove, CA, May 2007.

Swenson CN, Tomich DJ, Gomes JP. Evaluation of a mandated conversion of patients on ramipril and amlodipine to alternative agents at Madigan Army Medical Center. Presented at American Society of Health System Pharmacists, Midyear Clinical Mtg, Anaheim, CA, December 2006.

## **Physical Medicine & Rehabilitation Service**

Clouse D. NATA Workshop. Presented at NATA, Anaheim, CA, June 2007.

Harrison-Weaver S. War, What is it good for? Historical contribution of the military and war to occupational therapy and hand therapy. Presented at American Society of Hand Therapists 30th Annual Meeting, Phoenix, AZ, October 2007.

## **Department of Preventive Medicine**

Badzik DA. Hearing Loss in U.S. Army Aviators, Comparing 2001 to 2005. Presented at Research Day at University of Washington, Seattle, WA, May 2007.

Barraza EM, Hawthorne CL. Implementing a Tobacco Free Campus. Presented at USACHPPM Force Protection Conference - Health Promotion Track, Louisville, KY, August 2007.

Erickson KE. Co-morbidity of Migraine and Psychiatric Conditions in U.S. Army Soldiers Returning from Combat. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Erickson KE, Lucenko BA, Gahm GA, Erickson JC. Co-Morbidity of Migraine and Psychiatric Conditions in U.S. Army Soldiers Returning from Combat. Presented at 59th Annual Meeting of the American Academy of Neurology, Boston, MA, May 2007.

LaFon SG. An Outbreak of Plasmodium vivax Malaria among US Army Engineers Who Deployed to Afghanistan 2005-2006. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

LaFon SG, Scoville SL, Littell C, Gavrilis P, Weg A. An Outbreak of Plasmodium vivax Malaria among US Army Engineers who deployed to Afghanistan, 2005-2006. Presented at Force Health Protection Conference, Louisville, KY, August 2007.

## **Department of Psychiatry**

Reger G, Gahm GA, Rizzo A, Lucenko B, Reger MA, Swanson R, Deering S, Onorati K, Duma S. Enhancing Presence for PTSD Treatment: Soldier Feedback for the Virtual Iraq. Presented at American Telemedicine Association, Nashville, TN, May 2007.

## **Department of Psychology**

Duma SJ. Reset Project: A Post-Deployment, Behavioral Health Reset Personal Coach. Presented at Force Health Protection, Louisville, KY, August 2007.

Fritch AM. The Impact of Multiple Traumas Upon Mental Health Outcomes of Soldiers Returning from Deployment. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Gahm GA. Post Deployment Online: PTSD Project. Presented at Military Suicide Prevention Conference, Hollywood, FL, March 2007.

Gahm GA. Post Deployment Online PTSD Project. Presented at USA CHPPM, Force Health Protection Conference, Louisville, KY, August 2007.

Gahm GA. Soldier Wellness Assessment Pilot Program (SWAPP). Presented at Force Health Protection, Louisville, KY, August 2007.

Gahm GA, Reger MA, Crow BE. AMEDD Suicide Prevention Strategy. Presented at Military Suicide Prevention Conference, Hollywood, FL, March 2007.

Reger GM. Virtual Reality. Presented at CyberTherapy, Washington, DC, June 2007.

Reger GM. Virtual Reality in the Context of Operational Psychology. Presented at International Society for Traumatic Stress Studies (ISTSS), Hollywood, CA, November 2006.

## **Department of Radiology**

Cote MG. Bones, Breaks, and Groans. Presented at 31st Annual Western Regional Meeting, Society of Nuclear Medicine Representative, Reno, NV, October 2006.

Cote MG. PET/CT: The Best of Both Worlds in Molecular Imaging. Presented at Washington Association for Medical Transcriptionists, Tacoma, WA, April 2007.

Naeem M. Magnetic Resonance Cholangiopancreatography. Presented at Spring Medical Surgical Behavioral Science Conference, Bad Kissingen, Germany, March 2007.

Park MH. Retrospective Evaluation of Endovascular Interventions for War Related Extremity Injuries at Madigan Army Medical Center. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Statler JD. Terrorism and the Radiologist. Presented at Radiologic Society of North America, Chicago, Ill, November 2006.

## **General Surgery Service, Department of Surgery**

Arthurs Z, Cuadrado D, Sohn V, Lesperance K, Wolcott, K, Carter P, Sebesta J. Post-bariatric Panniculectomy: Pre-operative BMI Impacts the Complication Profile. Presented at North Pacific Surgical Association, Spokane, WA, November 2006.

Arthurs ZM, Andersen CA, Sohn VY, Perry JT, Mullenix PS, Starnes B. A Prospective Evaluation of C-Reactive Protein in the Progression of Carotid Artery Stenosis. Presented at Western Vascular Society 22nd Annual Meeting, Kona, HI, September 2007.

Bender BJ. Evaluating the Coding and Workload Accounting Improvement Initiative at Madigan Army Medical Center. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Cuadrado DG. Is Gastric Bypass Safe and Effective in Older Morbidly Obese Patients? Presented at Pacific Coast Surgical Association 78th Annual Scientific Program Meeting, Kohala Coast, HI, February 2007.

Herbert GS. Improved Accuracy with the 11-Gauge Vacuum-Assisted versus the 14-Gauge Core Biopsy Needle. Presented at Society of Surgical Oncology 2007 Cancer Symposium, Washington, DC, March 2007.

Herbert GS. Surgical Treatment of Lobular Neoplasia. Presented at Washington State Chapter American College of Surgeons, Chelan, WA, June 2007.

Herbert GS, Sohn VY, Brown TA. Prognostic Significance of Reactivation of Telomerase in Breast Core Biopsy Specimen. Presented at North Pacific Surgical Association, Spokane, WA, November 2006.

Herbert GS, Sohn VY, Brown TA. The Impact of Nodal Isolated Tumor Cells on Survival of Breast Cancer Patients. Presented at North Pacific Surgical Association, Spokane, WA, November 2006.

Kalbfleisch KA. Inhalation of methanol containing products - a significant source of toxicity. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Kidd MC, Mercer R, Erickson J. Does Stroke Education Increase Stroke Knowledge in an At Risk Population? Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Lehmann RK. Trauma Team Activation: Simplified Criteria Safely Reduces Over-triage. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Lehmann RK, Arthurs Z, Cuadrado D, Cassey LE, Beekley AC, Martin MJ. Trauma Team Activation: Simplified Criteria Safely Reduces Over-triage. Presented at North Pacific Surgical Association, Spokane, WA, November 2006.

Perry JT. Prevalence of Metabolic Syndrome in US Army Snior Soldiers. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Perry JT, Eckert MJ, Martin MJ, Sohn VY, Steele SR. Ischemic Colitis Complicating Open vs. Endovascular Abdominal Aortic Aneurysm Repair. Presented at American College of Surgeons 93rd Annual Clinical Congress, New Orleans, LA, October 2007.

Sapp JE, Mulhall BP, Reed RD. An Unusual Presentation of Metastatic Small Cell Bladder Carcinoma. Presented at A/AF American College of Physicians Annual Session, San Antonio, TX, USA, November 2007.

Sohn VY. Breast Papillomas in the Era of Percutaneous Needle Biopsy. Presented at Society of Surgical Oncology 2007 Cancer Symposium, Washington, DC, March 2007.

Sohn VY. Breast Papillomas in the Era of Percutaneous Needle Biopsy. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Sohn VY. Examples of IEDS. Presented at Pacific Coast Surgical Association, Kohala Coast, HI, February 2007.

Sohn VY, Eckert MJ, Perry JT, Beekley AC, Martin MJ, Rubel E, Adams R, Hassell J, Rush RM. Efficacy of Two Hemostatic Dressings Applied by Medics in a Lethal Groin Injury. Presented at Washington State Chapter American College of Surgeons, Chelan, WA, June 2007.

Sohn VY, Starnes B, Andersen C. Mid Aortic Syndrome and Renovascular Hypertension in a 14 year old Iraqi Girl: Pitfalls in Diagnosis and Surgical Management. Presented at North Pacific Surgical Association, Spokane, WA, November 2006.

Steele SR. Recurrent Rectal Prolapse. Presented at American College of Surgeons, Chicago, IL, October 2006.

Weisgram BK. Nursing 101: Using Evidence-Based Nursing Rounds to Improve Patient outcomes. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

### **Ophthalmology Service, Department of Surgery**

Amacher AG, Mazzoli RA, Raymond WR. Observations of Subperiosteal Injection for Endoscopic Browpexy Surgery. Presented at Association for Research in Vision and Ophthalmology (ARVO) Annual Conf., Fort Lauderdale, FL, May 2007.

Boden J, Lee T, Bushley DM, Myers ML, Torres M. The use of Lidocaine gel prior to Povidone - Iodine Antisepsis and its effect on Microbial Survivability. Presented at American Society of Catract and Refractive Surgery / Symposium on Cataract, IOL and Refractive Surgery, San Diego, CA, April 2007.

Davis RW. Health Promotions in Honduras. Presented at Madigan Research Day, Ft. Lewis, WA, April 2007.

Raymond WR, Mazzoli RA, Solverson DJ. Differentiating Basic Ophthalmic Microsurgical Skills Using Virtual Reality (VR) Simulation. Presented at Association for Research in Vision and Ophthalmology (ARVO) Annual Conference, Fort Lauderdale, FL, May 2007.

Solverson DJ, Mazzoli RA, Raymond WR, Nelson ML, Azarow KS, Torres MF, Hartranft CD. Virtual Reality Simulation in Acquiring Basic Ophthalmic Microsurgical Skills. Presented at American Academy of Ophthalmology, Las Vegas, NV, November 2006.

### **Orthopedics Service, Department of Surgery**

Antosh IJ, Grassbaugh JA, Arrington ED, Parada SA. Pectoralis Major Repairs in Active Duty Soldiers. Presented at Society of Military Orthopedic Surgeons, Honolulu, HI, December 2006.

Eichinger JK, Arrington ED, Herzog JP, Vining NC, Wright JR. Analysis of the Mechanical Properties of Locking Plates with and without Screw Hole Inserts. Presented at Society of Military Orthopaedic Surgeons, Honolulu, HI, December 2006.

Eichinger JK, Herzog JP, Vining NC, Arrington ED. Analysis of the Mechanical Properties of Locking Plates with and without Screw Hole Inserts. Presented at Western Orthopaedic Association Annual Meeting, San Diego, CA, July 2007.

Herzog JP, Arrington ED, White DW. A Retrospective Review of Post-Operative Shoulder Pain. Presented at Western Orthopedics Association, Santa Fe, NM, October 2006.

Herzog JP, Arrington ED, White DW. Post-Operative Shoulder Pain: A Prospective Randomized Trial Comparing the Pain Control Infusion Pump to the Pre-Induction Interscalene Block. Presented at Western Orthopedics Association, Santa Fe, NM, October 2006.

Schade VL, Sweet KJ. A Modification which Optimizes the Advantages of the Proximal Crescentic Osteotomy. Presented at Annual Meeting of American College of Foot and Ankle Surgeons, Orlando, FL, March 2007.

### **Otolaryngology Service, Department of Surgery**

Crawford JV, Spear SA. Comparison of Smart crimp & traditional crimp stapes pistons: A cadaver study. Presented at American Academy of Otolaryngology Head and Neck Surgery National Mtg, Washington DC, September 2007.

Demars SM, Esquivel CR, Backous DD. Review of postoperative complications after BAHA implantation at Madigan Army Medical Center and Virginia Mason Medical Center. Presented at Triological Society Meeting, Marco Island, FL, February 2007.

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## K. Exempt Protocols (no detailed summary sheet)

Number	PI	Dept/Serv	Protocol Title
207004	McCarthy MS	Nursing	Intensive Care Nurses' Knowledge and Assessment of Delirium in Elderly Critically Ill Patients
207013	Lesperance KE	Surgery/General	Trends in Operative Management of Ruptured Abdominal Aortic Aneurysms: A National Population Based Analysis
207015	Reyes SD	Nursing	Implementation and Evaluation of the Addition of a Virtual Reality System in Teaching Intravenous Initiation Skills to 91WM6 Practical Nurse Course Students
207016	Rosen IM	Family Medicine	Evaluating Young Military Women's Knowledge of Chlamydia and Identifying the Most Prevalent Sexual Risk Taking Behaviors within This Population
207034	Ney JP	Medicine/Neurology	Patient Expectations and Perceptions Prior to Nerve Conductions and Needle EMG
207036	Spear SA	Surgery/Otolaryngology	Comparison of smart crimp versus traditional crimp of stapes prosthesis: A cadaver study
207039	Sweet KJ	Surgery	The Use of Locking Plate and Compression Screw for Fixation of Proximal First Metatarsal Crescentic Osteotomy: A Mechanical Comparison of Three Fixation Constructs
207040	Roukis TS	Surgery/Vascular	Biomechanical Comparison of Two Crossed Screws Versus Locking Plate and Screws For First Metatarsophalangeal Joint Arthrodesis
207041	Roukis TS	Surgery/Vascular	Biomechanical Comparison of Three Different Lateral Wall Exit Levels for the First Metatarsal Z-Shaped Osteotomy Fixated with Threaded Head Screws
207042	Roukis TS	Surgery/Vascular	Biomechanical Comparison of Three Different Anatomically Contoured Locking Plate and Screw Configurations for First Metatarsocuneiform Arthrodesis
207043	Roukis TS	Surgery/Vascular	Biomechanical Comparison of Axial Screw Versus Plate with Locking Screws for the Oblique and Z-shaped Medial Calcaneal Displacement Osteotomies
207047	Foglia LM	OB/GYN	Proteomic Analysis of Protein Secretion from LTA-Treated Umbilical Cord White Blood Cells
207050	Liesemer EM	Pediatrics	Factors Influencing Acceptability of HPV Vaccine
207062	Flynn DM	Family Medicine	Impact of Case Management of Patients with Chronic Pain Taking High-Dose Opioid Medications
207066	Perry JT	Surgery/General	Nationwide Analysis of the Incidence of Ischemic Colitis Following Open Abdominal Aortic Aneurysm Repair and Endovascular Aortic Aneurysm Repair
207072	Reger MA	Psychology	Soldier Technology Use Survey
207084	Hopkins-Chadwick DL	Nursing	Evaluation of Nurses' Perceptions about the Use of Electronic Health Record (Essentris)
207100	Rivero CL	Nursing	SIDS: Health Professional's Knowledge and Parent Education
207106	Brehmer JI	Nursing	MAMC Patient/Family Team STEPPS Initiative Survey - Pre and Post Implementation
207109	Saunders RD	OB/GYN	The Effects of N-Acetylcysteine on the Production of Inflammatory Cytokines in a Placental Artery Explant Model
207121	Duma SJ	Psychology	Behavioral Health Screening and Soldier Mental Health Reset
207122	Jones TL	Nursing	The Effects of Individual Emotional Intelligence and Group Emotional Competence on Active Duty Military and Civilian Nurse-to-Nurse Hostility and Confrontational Anxiety: An Integral, Descriptive Study

## L. Detail Summary Sheets

### Table of Contents for Detail Summary Sheets

**Legend:** S = Status [O – Ongoing, C – Completed, T – Terminated]

T = Protocol Type [A – Animal, B – Bench, L – Local, M – Multicenter, R- Retrospective]

Prin. Invest.                      S   T   Title  
#Protocol No.

#### Department of Clinical Investigation

Bullock JM #206122	O A	Profiling of Proteins Extracted from Tissue Taken from Regenerating and Intact Notophthalmus viridescens Limbs Using SELDI
Hartenstine MJ #204100	T L	Human Blood Collection for Bench Research Initiatives
Hartenstine MJ #205031	O L	Proteomic Analysis of Longitudinally-Collected Maternal Plasma Samples: Establishing the 'Pregnancy Proteome'
Hartenstine MJ #205044	T L	A Prospective Study of Pseudocholinesterase Activity in Patients with Fibromyalgia, Chronic Pain, Pelvic Pain and Hernias
Merrill NL #206091	O A	MAMC Rodent and Rabbit Quality Assurance and Sentinel Program
Merrill NL #206109	O A	Animal Tissue Use in Biomedical Research and Training

#### Hospital Dental Clinic

Burgan SC #203116	T M	Host Response Gene 203014 in Military Populations
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#### Department of Emergency Medicine

Allan NN #206063	O L	A Randomized Study of Capnography in Emergency Department Procedural Sedation
Denny MA #207017	C L	Retrospective Review of Emergency Department Deep Sedation Cases at One Military Medical Center
Kang CS #207019	O L	Impact of the ACGME Outcomes Project on Emergency Medicine Residencies
Knutson TL #207024	O L	A pilot study of maximum safe 2-3 hour serum acetaminophen levels in comparison to standard 4-hour levels in acetaminophen overdose
Mullen NB #207092	O L	Effects of Intranasal Oxymetazoline on Pediatric Population 1-12 Months
Nielson AS #206059	C L	Causes and consequences of patients who left a busy Army Medical Center Emergency Department prior to evaluation by a qualified health care provider
Younggren BN #206078	O A	Emergency Medicine/Combat Trauma Management Training Using Animal Models (Domestic Goat/ Capra hircus, Pig/Sus scrofa)

#### Department of Family Medicine

Clark GW #205133	C L	Prevalence of Hypertension in Active Duty Service Members
Clark JC #207118	O L	Cervical Abnormalities in Routine Papanicolaou Smears in Women Over Age 65
Crosland T #205124	C L	Racial Differences in Health Outcomes for Adults with Diabetes in a Military Setting
Flynn DM #204117	C L	Impact of the Sole Prescriber Program on Use of Opioid Medications and Quality of Life

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<u>Prin. Invest.</u> <u>#Protocol No.</u>	<u>S</u>	<u>T</u>	<u>Title</u>
Flynn DM #206105	O	L	Implementation of an Office-Based Screening Tool to Improve Adherence with Recommended Preventive Services in Primary Care
Flynn DM #207001	O	L	Cardiovascular Risk Factor Identification in Active Duty Soldiers Over the Age of 40 Years
Johnson JD #207116	O	L	Urine Culture in the Primary Care Management of Urinary Tract Infections in Adult Females: Does it Decrease Follow-up Visits?
Kelly KM #205130	O	L	Use of Pedometers Among Healthcare Providers in a Large Military Family Medicine Department
Maurer DM #206048	C	L	A Randomized, Controlled Trial of Manual/Manipulative Therapy for Acute Low Back Pain in Active Duty Military Personnel: A Pilot Study
Michels TC #207006	O	M	Analysis of End-of-Life Care in Elderly Military Beneficiaries: A Pilot Study
Sams RW #206104	O	L	Implementing a Medical Ethics Curriculum in a Family Medicine Residency: Assessment of Need, Description of the Process, and Evaluation of Effectiveness
Short MW #206080	O	L	Predicting Intern Performance using an Objective Structured Clinical Examination
Short MW #207012	O	L	Colonoscopy by a Family Physician: A Case Series Comparing a Family Physician to a Gastroenterologist to Competency Standards

### Health Outcomes Management Division

Meyer JG #205108	T	L	The Deployment of Physical Therapy for Combat: A Description of the Process and Outcomes
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### Allergy/Immunology Service, Department of Medicine

Song TT #207061	C	L	Identification of Patients Prescribed B-blocker During Allergen Immunotherapy Without Allergist's Notification
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### Cardiology Service, Department of Medicine

Kinney KG #207068	T	M	Randomized, multinational, double-blind study comparing a high loading dose regimen of clopidogrel versus standard dose in patients with unstable angina or non-ST segment elevation myocardial infarction managed with an early invasive strategy (OASIS 7)
Schachter DT #201300	O	H	Jostent Coronary Stent Graft (HUD)
Schachter DT #202300	T	H	CardioSEAL Septal Occlusion System (HUD)

### Hematology/Oncology Service, Department of Medicine

Daniels JT #90027	O	S	SWOG 8851 (EST 5811, INT-0101): Phase III Comparison of Combination Chemotherapy (CAF) and Chemohormonal Therapy (CAF + Zoladex or CAF + Zoladex + Tamoxifen) in Premenopausal Women with Axillary Node-Positive, Receptor- Positive Breast Cancer
Daniels JT #91094	O	S	SWOG S9007 (ECOG S9007), Cytogenetic Studies in Leukemia Patients

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T = Protocol Type [A – Animal, B – Bench, L – Local, M – Multicenter, R- Retrospective]

<u>Prin. Invest.</u> <u>#Protocol No.</u>	<u>S</u>	<u>T</u>	<u>Title</u>
Daniels JT #93032	O	S	SWOG 9061 (EST-2190, INT 0121): A Phase III Study of Conventional Adjuvant Chemotherapy vs High Dose Chemotherapy and Autologous Bone Marrow Transplantation or Stem Cell Transplantation as Adjuvant Intensification Therapy Following Conventional Adjuvant Chemotherapy in Patients with Stage II and III Breast Cancer at High Risk of Recurrence
Daniels JT #93097	T	S	SWOG 9205: Central Prostate Cancer Serum Repository Protocol
Daniels JT #93136	C	S	SWOG 9221, MDACC ID 91-025, INT-191-001: Phase III Double-Blind Randomized Trial of 13-Cis Retinoic Acid (13-cRA) to Prevent Second Primary Tumors (SPTs) in Stage I Non-Small Cell Lung Cancer
Daniels JT #93166	O	S	SWOG 9303: Phase III Study of Radiation Therapy, Levamisole, and 5-Fluorouracil versus 5-Fluorouracil and Levamisole in Selected Patients With Completely Resected Colon Cancer
Daniels JT #94163	O	S	SWOG 9410 (INT 0148): Doxorubicin Dose Escalation, With or Without Taxol, As Part of the CA Adjuvant Chemotherapy Regimen for Node Positive Breast Cancer: A Phase III Intergroup Study
Daniels JT #95003	O	S	SWOG 9401: A Controlled Phase III Evaluation of 5-FU Combined with Levamisole and Leucovorin as Surgical Adjuvant Treatment Following Total Gross Resection of Metastatic Colorectal Cancer
Daniels JT #95093	O	S	SWOG 9402: Phase III Intergroup Randomized Comparison of Radiation Alone vs Pre-Radiation Chemotherapy for Pure and Mixed Anaplastic Oligodendrogliomas
Daniels JT #96095	O	S	SWOG 9514: Phase III Double-Blind, Placebo-Controlled, Prospective Randomized Comparison of Adjuvant Therapy with Tamoxifen vs. Tamoxifen & Fenretinide in Postmenopausal Women with Involved Axillary Lymph Nodes and Positive Receptors, Intergroup
Daniels JT #96118	C	S	SWOG 9515: Phase III Intergroup Trial of Surgery Followed by (1) Radiotherapy vs. (2) Radiochemotherapy for Resectable High Risk Squamous Cell Carcinoma of the Head and Neck
Daniels JT #97070	O	S	SWOG JBR.10 (NCIC CTG BR.10): A Phase III Prospective Randomized Study of Adjuvant Chemotherapy with Vinorelbine and Cisplatin in Completely Resected Non-small Cell Lung Cancer with Companion Tumour
Daniels JT #97096	C	S	SWOG 9059 (E1392, INT-0126): Phase III Comparison of Standard Radiotherapy versus Radiotherapy plus Simultaneous Cisplatin, versus, split-Course Radiotherapy plus Simultaneous Cisplatin and 5-Fluorouracil, in Patients with Unresectable Squamous Cell Carcinoma of the Head and Neck
Daniels JT #98112	O	S	SWOG C9581: Phase III Randomized Study of Adjuvant Immunotherapy with Monoclonal Antibody 17-1A Versus No Adjuvant Therapy Following Resection for Stage II (Modified Astler-Coller B2) Adenocarcinoma
Daniels JT #99014	O	S	SWOG C9741: A Randomized Phase III Trial of Sequential Chemotherapy Using Doxorubicin, Paclitaxel, and Cyclophosphamide, or Concurrent Doxorubicin and Cyclophosphamide Followed by Paclitaxel at 14 or 21 Day Intervals in Women with Node Positive Stage II/IIIA Breast Cancer

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<u>Prin. Invest.</u> <u>#Protocol No.</u>	<u>S</u>	<u>T</u>	<u>Title</u>
Daniels JT #99019	O	S	SWOG S9808: Long-Term Follow-Up Protocol: An Administrative Tool
Daniels JT #99040	O	S	SWOG JMA.17: A Phase III Randomized Double-Blinded Study of Letrozole Versus Placebo in Women with Primary Breast Cancer Completing Five or More Years of Adjuvant Tamoxifen
Daniels JT #99071	O	S	SWOG E2197: Phase III Study of Adriamycin/Taxotere vs. Adriamycin/Cytosan for the Adjuvant Treatment of Node Positive or High Risk Node Negative Breast Cancer
Daniels JT #200036	O	S	SWOG E1199: A Phase III Study of Doxorubicin-Cyclophosphamide Therapy Followed by Paclitaxel or Docetaxel Given Weekly or Every 3 Weeks in Patients with Axillary Node-Positive Breast Cancer
Daniels JT #200040	O	S	SWOG E4494: Phase III Trial of CHOP versus CHOP and Chimeric Anti-CD20 Monoclonal Antibody (IDEC-C2B8) in Older Patients with Diffuse Mixed, Diffuse Large Cell and Immunoblastic Large Cell Histology Non-Hodgkin's Lymphoma
Daniels JT #200084	O	S	SWOG S9921: Adjuvant Androgen Deprivation versus Mitoxantrone plus Prednisone plus Androgen Deprivation in Selected High Risk Prostate Cancer Patients Following Radical Prostatectomy, Phase III
Daniels JT #200120	O	S	SWOG N9831: Phase III Trial of Doxorubicin and Cyclophosphamide (AC) Followed by Weekly Paclitaxel With or Without Trastuzumab as Adjuvant Treatment for Women with HER-2 Over-expressing or Amplified Node Positive or High-Risk Node Negative Breast Cancer (an Intergroup Study)
Daniels JT #201137	O	S	SWOG S0012: A Comparative Randomized Study of Standard Doxorubicin and Cyclophosphamide Followed by Weekly Paclitaxel Vs. Weekly Doxorubicin and Daily Oral Cyclophosphamide Plus G-CSF Followed by Weekly Paclitaxel as Neoadjuvant Therapy for Inflammatory and Locally Advanced Breast Cancer
Daniels JT #202010	O	S	SWOG E5597: Phase III Chemoprevention Trial of Selenium Supplementation in Persons with Resected Stage I Non-Small Cell Lung Cancer
Daniels JT #202012	O	S	SWOG GO182: A Phase III Randomized Trial of Paclitaxel and Carboplatin Versus Triplet or Sequential Doublet Combinations in Patients with Epithelial Ovarian or Primary Peritoneal Carcinoma
Daniels JT #202074	O	S	SWOG S9925 Lung Cancer Specimen Repository Protocol, Ancillary
Daniels JT #203084	O	S	SWOG S0016, A Phase III Trial of CHOP + Rituximab vs. CHOP + Iodine-131-Labeled Monoclonal Anti-B1 Antibody (Tositumomab) for Treatment of Newly Diagnosed Follicular Non-Hodgkin's Lymphomas
Daniels JT #204034	O	S	SWOG S0221, Phase III Trial of Continuous Schedule AC + G Vs. Q 2 Week Schedule AC, Followed by Paclitaxel Given Either Every 2 Weeks or Weekly for 12 Weeks as Post-Operative Adjuvant Therapy in Node-Positive or High-Risk Node-Negative Breast Cancer
Daniels JT #204064	O	S	SWOG S0230, Phase III Trial of LHRH Analog Administration During Chemotherapy to Reduce Ovarian Failure Following Chemotherapy in Early Stage, Hormone- Receptor Negative Breast Cancer



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Daniels JT #204066	O	S	SWOG E2496: Randomized Phase III Trial of ABVD Versus Stanford V +/- Radiation Therapy in Locally Extensive and Advanced Stage Hodgkin's Disease With 0-2 Risk Factors
Daniels JT #204094	O	S	SWOG S0226, Phase III Randomized Trial of Anastrozole Versus Anastrozole and Fulvestrant as First Line Therapy for Post Menopausal Women With Metastatic Breast Cancer
Daniels JT #204123	O	S	SWOG S0106, A Phase III Study of the Addition of Gemtuzumab Ozogamicin (Mylotarg®) During Induction Therapy Versus Standard Induction With Daunomycin and Cytosine Arabinoside Followed by Consolidation and Subsequent Randomization to Post-Consolidation Therapy With Gemtuzumab Ozogamicin (Mylotarg®) or No Additional Therapy for Patients Under Age 56 With Previously Untreated DeNovo Acute Myeloid Leukemia (AML)
Daniels JT #205007	O	M	PSOC 2003: A Phase II Study Evaluating the Efficacy of Gemcitabine, Carboplatin, Dexamethasone and Rituximab for Previously Treated Lymphoid Malignancies, UW Protocol Number LYM.03.01
Daniels JT #205035	O	S	SWOG S9910 Leukemia Centralized Reference Laboratories and Tissue Repositories, Ancillary
Daniels JT #206023	T	M	A Multi-Center, Randomized, Phase 3 Study of Iodine I-131 Tositumomab Therapeutic Regimen Versus Ibritumomab Tiuxetan Therapeutic Regimen for Subjects with Relapsed or Transformed Follicular Non-Hodgkin's Lymphoma
Daniels JT #206068	O	S	SWOG S0520: Phase II Study of PXD101 (NSC-726630) in Relapsed and Refractory Aggressive B-Cell Lymphomas
Daniels JT #207054	O	M	CALGB 80101: Phase III Intergroup Trial of Adjuvant Chemoradiation after Resection of Gastric or Gastroesophageal Adenocarcinoma
Daniels JT #207055	O	S	CTSU E5204, Intergroup Randomized Phase III Study of Postoperative Oxaliplatin, 5-Fluorouracil and Leucovorin vs. Oxaliplatin, 5-Fluorouracil, Leucovorin and Bevacizumab for Patients with Stage II or III Rectal Cancer Receiving Pre-operative Chemoradiation
Daniels JT #207067	O	S	CALGB 50303: Phase III Randomized Study of R-CHOP VS Dose-Adjusted EPOCH-R with Molecular Profiling in Untreated De Novo Diffuse Large B-Cell Lymphomas
McCune DE #202043	C	S	CTSU RTOG 98-04: Phase III Trial of Observation +/- Tamoxifen vs. RT +/- Tamoxifen for Good Risk Duct Carcinoma In-Situ (DCIS) of the Female Breast
McCune DE #202083	C	M	A Randomized Phase III Trial of Gemzar versus Doxil with Crossover Treatment Option for Patients with Platinum-Resistant Ovarian, Fallopian Tube or Primary Peritoneal Cancer Undergoing Second or Third-Line Chemotherapy, Protocol Number: B9E-US-S301
McCune DE #202088	C	S	CTSU E1A00 A Randomized Phase III Trial of Thalidomide (NSC #66847) Plus Dexamethasone versus Dexamethasone in Newly Diagnosed Multiple Myeloma

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McCune DE #202089	C	S	CTSU CALGB 49907, A Randomized Trial of Adjuvant Chemotherapy With Standard Regimens, Cyclophosphamide, Methotrexate and Fluorouracil - (CMF) or Doxorubicin and Cyclophosphamide - (AC), Versus Capecitabine in Women 65 Years and Older with Node Positive or Node Negative Breast Cancer
McCune DE #202114	O	S	CTSU CALGB 40101, Cyclophosphamide and Doxorubicin (CA) (4 VS 6 Cycles) versus Paclitaxel (4 VS 6 Cycles) as Adjuvant Therapy for Women with 0-3 Positive Axillary Lymph Nodes: A 2X2 Factorial Phase III Randomized Study
McCune DE #204008	O	M	Phase II Trial of ONTAK® in Refractory or Relapsed Advanced Non-small Cell Lung Cancer (NSCLC)
McCune DE #204035	O	S	CTSU NCIC CTG MA.27, A Randomized Phase III Trial of Exemestane Versus Anastrozole in Postmenopausal Women With Receptor Positive Primary Breast Cancer
McCune DE #204043	O	S	CTSU IBCSG Trial 25-02, Tamoxifen and Exemestane Trial (TEXT), A Phase III Trial Evaluating the Role of Exemestane Plus GnRH Analogue as Adjuvant Therapy for Premenopausal Women with Endocrine Responsive Breast Cancer
McCune DE #204044	O	M	A Phase III Study of Delayed vs. Immediate Second-line Therapy with Docetaxel after Gemcitabine + Carboplatin in Advanced Non-Small Cell Lung Cancer, Protocol Number B9E-US-S245
McCune DE #204073	C	M	A Multicenter, Randomized, Phase III Study of Rituximab versus Iodine I 131 Tositumomab Therapeutic Regimen for Patients with Relapsed Follicular Non-Hodgkin's Lymphoma, Protocol CCBX001-049
McCune DE #204080	O	M	Protocol U2963n: The National Lymphocare Study: An Observational Study of Treatment, Outcomes, and Prognosis in Patients With Follicular Non-Hodgkin's Lymphoma
McCune DE #204107	O	S	CTSU ACOSOG-Z9001, A Phase III Randomized Double-blind Study of Adjuvant STI571 (Gleevec™) Versus Placebo in Patients Following the Resection of Primary Gastrointestinal Stromal Tumor (GIST)
McCune DE #204114	O	M	A Phase II Trial of Weekly Docetaxel plus Every 3-Week Carboplatin in Patients with Stage IIIB/IV Non-small Cell Lung Cancer, Protocol GIA 12156
McCune DE #205070	T	M	A Phase II Study Using Alemtuzumab Combined with Fludarabine for the Treatment of Relapsed/Refractory B-cell Chronic Lymphocytic Leukemia (B-CLL)
McCune DE #205087	O	M	A Phase II, Open Label, Multi-center Study of EP2101 Therapeutic Vaccine in Patients with Stage IIIB, Stage IV, or Recurrent Non-Small Cell Lung Cancer (NSCLC)
McCune DE #205093	C	M	A Phase 3, Double-Blind, Placebo-Controlled Study of Maintenance Premetrexed plus Best Supportive Care versus Best Supportive Care Immediately Following Induction Treatment for Advanced Non-Small Cell Lung Cancer AND COMPANION STUDY Companion Translational Research Protocol
McCune DE #206013	T	S	SWOG S0435 A Phase II Trial of BAY 43-9006 (SNC-724772) in Patients with Platinum-Treated Extensive Stage Small Cell Lung Cancer

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McCune DE #206014	C	M	A Phase I/II Trial of Zometa in Patients with Monoclonal Gammopathy of Undetermined Significance (MGUS)
McCune DE #206054	O	M	NSABP B-38 A Phase III Adjuvant Trial Comparing Three Chemotherapy Regimens in Women with Node-Positive Breast Cancer: Docetaxel/Doxorubicin/Cyclophosphamide (TAC); Dose-Dense (DD) Doxorubicin/Cyclophosphamide Followed by DD Paclitaxel (DD AC-P); DD Doxorubicin/Cyclophosphamide Followed by DD Paclitaxel Plus Gemcitabine (DD AC-PG)
McCune DE #206055	O	S	SWOG S0424: Molecular Epidemiology Case-Series Study of Non-Small Cell Lung Cancer in Smoking and Non-Smoking Women and Men
McCune DE #206073	T	M	Phase 1/2 study of ZK-Epothilone (ZK-Epo; ZK 219477) in combination with carboplatin in patients with platinum-sensitive, recurrent ovarian cancer
McCune DE #206084	T	M	Pilot Study to Evaluate the Safety and Efficacy of PROCRT (Epoetin alfa) 80,000 Units Once Every Four Weeks (Q4W) vs. 40,000 Units Once Every Two Weeks (Q2W) in Cancer Patients with Non-Chemotherapy Anemia
McCune DE #206112	O	G	CTSU GOG 0218, A Phase III Trial of Carboplatin and Paclitaxel Plus Placebo Versus Carboplatin and Paclitaxel Plus Concurrent Bevacizumab (NSC #704865, IND #7921) Followed By Placebo, Versus Carboplatin and Paclitaxel Plus Concurrent and Extended Bevacizumab, In Women With Newly Diagnosed, Previously Untreated, Stage III or IV Epithelial Ovarian or Primary Peritoneal Cancer
McCune DE #206126	O	L	A Phase II Trial of Imatinib (Gleevec) Plus Gemcitabine In Patients With Ovarian Carcinoma Who Have Failed At Least One Prior Chemotherapy
McCune DE #207023	T	M	Phase 2 study of ZK-Epothilone (ZK-Epo; ZK 219477) plus prednisone as first-line chemotherapy in patients with metastatic androgen-independent prostate cancer
McCune DE #207027	O	M	Prospective, Randomized, Single-Blinded, Multi-Center Phase II Trial of the HER2/neu Peptide GP2 + GM-CSF Vaccine versus GM-CSF Alone in HLA-A2+ OR the Modified HER2/neu Peptide AE37 + GM-CSF Vaccine versus GM-CSF alone in HLA-A2- Node-Positive and High-Risk Node-Negative Breast Cancer Patients to Prevent Recurrence
McCune DE #207077	O	L	CTSU CALGB 70301, Quality of Life, Employment and Informal Care Cost Analysis in Women Receiving Adjuvant Chemotherapy for Breast Cancer with 0-3 Positive Axillary Lymph Nodes Companion to CALGB 40101
McCune DE #207078	T	M	An Observational Study of Avastin® (Bevacizumab) in Combination with Chemotherapy for Treatment of Metastatic or Locally Advanced and Unresectable Colorectal Cancer, Locally Advanced or Metastatic Non-Small Cell Lung (Excluding Predominant Squamous Cell Histology), or Locally Recurrent or Metastatic Breast Cancer
McCune DE #207089	O	M	An international, randomised, double blind, placebo controlled, parallel group study to investigate whether TroVax, added to first-line standard of care therapy, prolongs the survival of patients with locally advanced or metastatic clear cell renal adenocarcinoma

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McCune DE #207090	T	M	A Randomized, Double-blind, Multicenter, Placebo-controlled Study of Adjuvant Lapatinib in Women with Early-Stage ErbB2 Overexpressing Breast Cancer
McCune DE #207110	O	L	Micronics Protocol for Typing 'Waste' Blood Samples from Madigan Army Medical Center
Mysliwiec AG #205036	O	S	CTSU NSABP C-08, A Phase III Clinical Trial Comparing Infusional 5-Fluorouracil (5-FU), Leucovorin, And Oxaliplatin (mFOLFOX6) Every Two Weeks With Bevacizumab To The Same Regimen Without Bevacizumab For The Treatment Of Patients With Resected Stages II And III Carcinoma of the Colon
Mysliwiec AG #207088	O	S	CTSU E2805, ASSURE: Adjuvant Sorafenib or Sunitinib for Unfavorable Renal Carcinoma
Mysliwiec AG #207097	O	S	CTSU CALGB 90401, A Randomized Double-Blinded Placebo Controlled Phase III Trial Comparing Docetaxel and Prednisone With and Without Bevacizumab (IND #7921, NSC #704865) in Men With Hormone Refractory Prostate Cancer
Mysliwiec AG #207098	O	S	CTSU NSABP B-42, A Clinical Trial to Determine the Efficacy of Five Years of Letrozole Compared to Placebo in Patients Completing Five Years of Hormonal Therapy Consisting of an Aromatase Inhibitor (AI) or Tamoxifen Followed by an AI in Prolonging Disease-Free Survival in Postmenopausal Women with Hormone Receptor Positive Breast Cancer
Ramsdell MJ #204082	C	L	Evaluating Cognitive Function in Women Receiving Chemotherapy for Newly Diagnosed Breast Cancer
Sebesta JA #206113	O	S	CTSU E5202: A Randomized Phase III Study Comparing 5-FU, Leucovorin and Oxaliplatin versus 5-FU, Leucovorin, Oxaliplatin and Bevacizumab in Patients with Stage II Colon Cancer at High Risk for Recurrence to Determine Prospectively the Prognostic Value of Molecular Markers

### Infectious Disease Service, Department of Medicine

Venkatarama RG #207123	O	L	Improving Patient Outcomes Using a Collaborative Hypertension Clinic
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### Internal Medicine Service, Department of Medicine

Allison JC #202048	O	M	A Multinational, Randomized, Double-blind, Placebo-controlled, Forced-titration, 2X2 Factorial Design Study of the Efficacy and Safety of Long Term Administration of Nateglinide and Valsartan in the Prevention of Diabetes and Cardiovascular Outcomes in Subjects with Impaired Glucose Tolerance (IGT), Protocol No. CDJN608 B2302
Allison JC #204045	O	M	A Prospective, Multinational, Multicenter Trial to Compare the Effects of Amlodipine/Benazepril to Benazepril and Hydrochlorothiazide Combined on the Reduction of Cardiovascular Morbidity and Mortality in Patients With High Risk Hypertension. Protocol No. CCIB002I2301: ACCOMPLISH (Avoiding Cardiovascular Events through COMbination Therapy in Patients Living with Systolic Hypertension)
Avalos C #205046	T	L	The Effect of Blood Transfusion on Serum Ferritin and Iron
Bauler KC #205123	O	L	Current Use and Complications of Peripherally Inserted Central Catheters (PICC): A Retrospective Study

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<u>Prin. Invest.</u> <u>#Protocol No.</u>	<u>S</u>	<u>T</u>	<u>Title</u>
Kwon HP #206069	O	L	The Effects of Nighttime Low Dose Aspirin on Ambulatory Blood Pressure Testing in Treated Hypertensive Patients
Kwon HP #206087	C	L	Hemoptysis in Young Adults
Papadopoulos PJ #205039	C	L	Management of Parapneumonic Effusions: Does Following Pneumonia Treatment Guidelines Affect Outcome? A Retrospective Study
Sapp JE #207060	O	L	Effect of Combination Treatment with Fluticasone/Salmeterol (Advair) and Tiotropium (Spiriva) on Pulmonary Function Tests, Hospital Admissions, and Documented Exacerbations of COPD at MAMC
Shelhamer MC #206119	O	L	Urinary Markers of Renal Injury and N-Acetylcysteine Efficacy (URINE)
Shelhamer MC #207021	O	L	Variation of Urinary Enzymes Gamma-Glutamyltransferase and N-Acetyl-Beta-D-Glucosaminidase in Patients Receiving N-Acetylcysteine
Short PA #207107	O	M	Geriatric Home Visit Program for Uniformed Services University MS3 students during their Internal Medicine Ambulatory Clerkship
Short PA #207108	O	M	The Impact of Electronic Evaluation Systems on the Quality of Resident Evaluations
Smith ME #207030	O	L	A Randomized Placebo Controlled Trial Investigating the Therapeutic Efficacy of Montelukast in the Treatment of Eosinophilic Esophagitis

### Neurology Service, Department of Medicine

Erickson JC #203048	T	L	A Randomized Trial of B Vitamins for Alzheimer's Disease
Erickson JC #203097	O	M	CLOSURE I Trial: A Prospective, Multicenter, Randomized, Controlled Trial to Evaluate the Safety and Efficacy of the STARFlex Septal Closure System Versus Best Medical Therapy in Patients with a Stroke and/or Transient Ischemic Attack Due to a Presumed Paradoxical Embolism Through a Patent Foramen Ovale
Erickson JC #204062	O	L	A Randomized Trial of a Migraine Management Seminar in the Treatment of Migraines
Erickson JC #205115	O	M	Study of Acute Viprinex™ for Emergency Stroke: A Randomized, Double-Blind, Placebo-Controlled Study of Viprinex™ (Ancrod Injection) in Subjects Beginning Treatment within 6 Hours of the Onset of Acute, Ischemic Stroke
Erickson JC #205118	O	L	Prevalence and Impact of Migraine Among Deployed Soldiers
Erickson JC #206075	O	L	Association Between Migraine and Psychiatric Conditions In Soldiers Returning from Combat
Erickson JC #207081	O	L	An Observational Study of Patients with Headache Disorders Referred for Neurology Specialty Care at a U.S. Army Medical Center
Ney JP #207104	O	L	Sural-Medial Plantar Electrodiagnostic Comparison Study for Tarsal Tunnel Syndrome-Reference Values

### Pulmonary Disease & Critical Care Service, Department of Medicine

Mysliwiec V #206086	O	L	Identifying Adherence Obstacles to CPAP Therapy
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Niven AS #205128	O	L	Impulse Oscillometry and Obstructive Lung Disease: Assessment of a Clinically Significant Bronchodilator Response
Niven AS #207093	O	L	Effect of Dried Garlic Supplements on Pulmonary Gas Exchange: A Prospective, Double Blinded, Crossover, Pilot Study
Niven AS #207094	O	M	A 26-week treatment, multicenter, randomized, double-Blind, double-Dummy, placebo-controlled, adaptive, seamless, parallel-group study to assess the efficacy, safety and tolerability of two doses of indacaterol (selected from 75, 150, 300, & 600 mcg o.d.) in patients with chronic obstructive pulmonary disease using blinded formoterol (12 mcg b.i.d.) and open label tiotropium (18 mcg o.d.) as active controls
Niven AS #207099	O	L	Evaluation of the Number and Variety of Procedures Done by Army General Internists: A Survey
<b>Nutrition Care Division</b>			
Geisler KL #207091	O	L	A Comparison of the Futrex-6100/XL Body Composition Analyzer and Dual Energy X-Ray Absorptiometry (DEXA) for Accuracy and Reliability of Percent Body Fat Measurement
Hartenstine MJ #206008	C	L	Attenuation of Exertional Muscle Damage with a Nutritional Supplement
<b>Department of Nursing</b>			
Connally TA #206093	O	L	Effects on Aspirated Volume, Patency, and Tracheal Mucosa using High Intermittent Negative Pressure versus Low Continuous Negative Pressure for Subglottic Secretion Aspiration
Feliciano WT #207101	C	L	A Retrospective, Exploratory Study Evaluating Incidence of Postoperative Urinary Retention (POUR) and Its Effect on Post-Anesthesia Care Unit (PACU) Discharge
Hodge NS #207086	O	L	A Prospective, Randomized Study of the Effectiveness of Aromatherapy for Relief of Postoperative Nausea & Vomiting
Hopkins-Chadwick DL #207076	C	L	Evaluation of the Sexual Awareness Kit (SAK)
Loan LA #201104	O	L	Newborn Infant Speech Perception
Loan LA #202066	C	L	Caring Interventions for Couples Who Have Miscarried
Loan LA #202075	O	L	Secondary Analysis of NICU Modified Care Environment Projects
Loan LA #204031	O	M	Military Nursing Outcomes Database: Analysis & Expansion (MilNOD IV)
Loan LA #204084	C	L	Impact of Inpatient Physician Order Entry on Medication Administration and Dispensing Error Rates in the Neonatal Intensive and Intermediate Care Units
Loan LA #205037	O	L	Determining the Effectiveness of a Stroke Prevention Program

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<u>Prin. Invest.</u> <u>#Protocol No.</u>	<u>S</u>	<u>T</u>	<u>Title</u>
Loan LA #205117	C	L	A Qualitative Descriptive Study that Identifies Essential Competencies and Leadership Characteristics of Army Adult Medical-Surgical Critical Care Head Nurses (dissertation)
Loan LA #207063	C	L	Patient Perceptions, Attitudes and Barriers to Using Water for Comfort in Labor and Birth (Pilot Study)
Loan LA #207120	O	L	Comparison of Cardiovascular Risk Factors in Deployed Military Personnel
McCarthy MS #207032	O	L	Bone Health in Soldiers Before and After Deployment
McNabb LA #206108	C	L	Army Nurse Corps Officers' Deployment Experiences and Reintegration
Trego LL #206107	O	L	Menstruation During Deployment: Women's Attitudes Towards Menstrual Suppression

### Department of Obstetrics/Gynecology

Chinn MK #205140	T	L	Continuous Use of the Oral Contraceptive for Menstrual Cycle Suppression and the Effects on Bone Density; a Prospective, Randomized, Clinical Trial
Dainty LA #81035	O	G	GOG 0041: Surgical Staging of Ovarian Carcinoma
Dainty LA #81105	O	G	GOG 0052: A Phase III Randomized Study of Cyclophosphamide Plus Adriamycin Plus Platinol Versus Cyclophosphamide Plus Platinol in Patients with Optimal Stage II Ovarian Adenocarcinoma
Dainty LA #84033	O	G	GOG 0072: Ovarian Tumors of Low Malignant Potential: A Study of the Natural History and a Phase II Trial of Melphalan and Secondary Treatment with Cisplatin in Patients with Progressive Disease
Dainty LA #84074	C	G	GOG 0078: Evaluation of Adjuvant VP-16, Bleomycin, and Cisplatin (BEP) Therapy in Totally Resected Choriocarcinoma, Endodermal Sinus Tumor, Embryonal Carcinoma and Grade 3 Immature Teratoma of the Ovary, Pure and Mixed with Other Elements
Dainty LA #86089	O	G	GOG 0085: A Randomized Comparison of Hydroxyurea versus 5-FU Infusion and Bolus Cisplatin as an Adjuvant to Radiation Therapy in Patients with Stages II-B, III, and IV-A Carcinoma of the Cervix and Negative Para-Aortic Nodes
Dainty LA #87028	O	G	GOG 0095: Randomized Clinical Trial for the Treatment of Women with Selected Stage IC and II (A,B,C) and Selected IAi and IBi and IAii and IBii Ovarian Cancer, Phase III
Dainty LA #87091	C	G	GOG 0099: A Phase III Randomized Study of Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma
Dainty LA #87104	C	G	GOG 0092: Treatment of Selected Patients with Stage 1B Carcinoma of the Cervix After Radical Hysterectomy and Pelvic Lymphadenectomy: Pelvic Radiation Therapy versus No Further Therapy
Dainty LA #93063	O	G	GOG 0123: A Randomized Comparison of Radiation Therapy & Adjuvant Hysterectomy vs Radiation Therapy & Weekly Cisplatin & Adjuvant Hysterectomy in Patients with Bulky Stage IB Carcinoma of the Cervix

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<u>Prin. Invest.</u> <u>#Protocol No.</u>	<u>S</u>	<u>T</u>	<u>Title</u>
Deering SH #206029	O	L	Simulation Training for Postpartum Hemorrhage
Flood SK #206098	T	L	Serum Estradiol Levels in Patients with Polycystic Ovarian Syndrome undergoing Ovulation Induction with Clomiphene Citrate
Hill DL #204111	T	M	Glyburide Compared to Insulin in the Management of White's Classification A2 Gestational Diabetes
Hill DL #206099	O	L	Molecular mechanisms of progesterone mediated inhibition of LPS and other inflammatory agent induced production of pro-inflammatory cytokines in the fetal-maternal circuitry of the human placenta
Howard BC #203066	O	L	The Production of Immunoregulatory Cytokines in a Placental Artery Explant Model
Howard BC #203067	T	L	The Effects of IL-10 on the Production of Inflammatory Cytokines in a Placental Artery Explant Model
Howard BC #204088	O	M	Use of Transvaginal Cervical Length Measurements in Twin Gestations
Lattu AL #203078	C	L	Use of Pipelle Endometrial Sampling in the Evaluation of Abnormal First Trimester Pregnancy
Lattu AL #205005	O	L	The Distribution of Bishop Scores and Quantitative Values of Fetal Fibronectin (fFN) in Nulliparous Patients Between 37-42 Weeks Gestation: A Prospective Observational Study
Lattu AL #207069	O	L	Resident Self-Assessment in Breast Examination Training
McPhee MM #205089	T	L	Pilot Study of a Novel Cord Blood Collection Technique
Napolitano PG #203001	O	B	The Effect of Magnesium on Matrix Metalloproteinase-9 Activity in Umbilical Cord Blood at Delivery of Pregnancies Complicated by Chorioamnionitis
Napolitano PG #203045	O	M	Randomized Controlled Trial of Endurance Exercise and Gallbladder Disease Risk in Overweight Pregnant Women
Napolitano PG #203099	O	L	Umbilical Cord Plasma Homocysteine Concentrations at Delivery in Pregnancies Complicated by Preeclampsia
Napolitano PG #207125	O	L	In Vivo Effects of Medroxyprogesterone Acetate on Lipopolysaccharide Induced IL-6 Expression and ERK-Kinase Activity
Perez CJ #207102	O	L	Prevalence, Risk Factors, and Common Organisms in Urinary Tract Infections in Urogynecologic Patients
Shen-Gunther J #207083	C	L	Operation Enduring Freedom: Trends in Combat Casualty Care by Forward Surgical Teams Deployed to Afghanistan
Vaccaro CM #205021	C	L	Correlation of Persistent Anal Sphincter Defects and Symptoms following Repair of Anal Sphincter Lacerations due to Obstetric Injury in Primiparous Women
Weeks LL #207085	O	L	Simulation Training to Evaluate the Force Used During Vaginal Delivery and Shoulder Dystocia



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### Department of Pathology

Champeaux AL #205042	C   L	Incidental Anatomic and Histologic Findings in Bariatric Surgery Specimens
Fernelius CA #205102	C   L	Absolute Lymphocytosis in Adults: A Laboratory Protocol
Viscount HB #203041	O   M	Use of a Non-FDA Approved Gene Amplification Test To Detect or Rule-Out Vaccinia in Patients With Complications Following Smallpox Vaccination or Possible Contact Vaccinia

### Department of Pediatrics

Barondeau JJ #207124	O   L	Safe Minimum Wrestling Weights: How Familiar are Health Care Providers with Means of Determining Safe Weights, and are Current Guidelines Practical in the Typical Outpatient Clinic Setting?
Cartwright VW #207025	O   L	Measuring Professionalism in Pediatric Residents: Feedback on Patient Encounter Videotaping
Davis BE #204074	C   M	Survey of Chronic Pain and Its Effects on Youth With Disabilities
Davis BE #204104	C   M	Health, Quality of Life & Activity in Cerebral Palsy
Ervin MK #206049	O   L	An Observational Study to Determine the Factors Influencing Bone Mineral Density in Post-Menarchal Adolescents with Neuromuscular Disabilities
Fairchok MP #205138	C   M	Evaluation of Serologic Responses to Fluzone® in Infants > 6 Months of Age Who Did or Did Not Receive Fluzone Vaccine at 2 Months of Age
Fairchok MP #205139	O   L	The Impact of Human Metapneumovirus Versus other Common Respiratory Viruses in Infants in Fulltime Daycare
Fairchok MP #207119	O   L	Utilizing Cerebral Spinal Fluid Polymerase Chain Reaction (CSF PCR) to Reveal Unsuspected Varicella-Zoster Meningitis
Fitzgerald KL #206035	C   M	Military Children at Risk - Enhancing Quality of Life (mCARE) Needs Assessment
Flake EM #207003	O   L	Effects of Deployment in Military Children on General Health, School Performance and Health Care Utilization
Forouhar MA #97054	O   C	POG 9426: Response Dependent Treatment of Stages IA, IIA, and IIIA(1-micro) Hodgkin's Disease with DBVE and Low Dose Involved Field Irradiation with or without Zinecard
Forouhar MA #98065	O   C	POG P9641: Primary Surgical Therapy for Biologically Defined Low-Risk Neuroblastoma; A COG Phase III Intergroup Study
Forouhar MA #98090	O   C	COG P9442: National Wilms Tumor Late Effects Study
Forouhar MA #200048	O   C	POG P9851: Osteosarcoma Biology Protocol, Companion to Group-Wide Therapeutic Studies
Forouhar MA #200049	O   C	COG D9902, A COG Soft Tissue Sarcoma Diagnosis, Biology and Banking Protocol
Forouhar MA #200076	O   C	COG 9905, ALinC 17: Protocol for Patients with Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL), A Phase III Study

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Forouhar MA #200077	O	C	COG 9904, ALinC 17: Treatment for Patients with Low Risk Acute Lymphoblastic Leukemia, A Phase III Study
Forouhar MA #200139	O	C	COG A5971: Randomized Phase III Study for the Treatment of Newly Diagnosed Disseminated Lymphoblastic Lymphoma or Localized Lymphoblastic Lymphoma, A Phase III COG Study
Forouhar MA #201108	O	C	COG ANBL00B1, Neuroblastoma Biology Studies
Forouhar MA #203024	O	C	COG AHOD0031, A Phase III Group-wide Study of Dose-intensive Response-based Chemotherapy and Radiation Therapy for Children and Adolescents with Newly Diagnosed Intermediate Risk Hodgkin Disease
Forouhar MA #205014	O	C	COG AHOD0321, A Phase II Study of Weekly Gemcitabine and Vinorelbine in Children with Recurrent or Refractory Hodgkin Disease
Forouhar MA #205015	O	C	COG AALL0031, A COG Pilot Study for the Treatment of Very High Risk Acute Lymphoblastic Leukemia in Children and Adolescents
Forouhar MA #205067	O	C	COG AALL03B1, Classification of Acute Lymphoblastic Leukemia
Forouhar MA #205068	O	C	COG AALL0232, High Risk B-precursor Acute Lymphoblastic Leukemia
Forouhar MA #205084	O	C	COG AGCT0132, A Phase III Study of Reduced Therapy in the Treatment of Children with Low and Intermediate Risk Extracranial Germ Cell Tumors
Forouhar MA #205095	O	C	COG AALL0331, Standard Risk B-precursor Acute Lymphoblastic Leukemia; A Phase III Group-Wide Study
Forouhar MA #205105	T	C	COG-LTF, A Groupwide Process for Collecting Long Term Follow Up Data
Forouhar MA #205110	O	C	COG AALL03N1, Understanding the Ethnic and Racial Differences in Survival in Children with Acute Lymphoblastic Leukemia
Forouhar MA #206034	C	C	COG ACNS0423: A Phase II Study of Concurrent Radiation and Temozolomide Followed by Temozolomide and Lomustine (CCNU) in the Treatment of Children with High Grade Glioma
Forouhar MA #206052	O	C	COG ACNS0331 A Study Evaluating Limited Target Volume Boost Irradiation and Reduced Dose Craniospinal Radiotherapy (18.00 Gy) and Chemotherapy in Children with Newly Diagnosed Standard Risk Medulloblastoma: A Phase III Double Randomized Trial
Forouhar MA #206095	O	C	COG AEWS02B1, A Group wide Biology and Banking Study for Ewing Sarcoma
Forouhar MA #206096	O	C	COG AHOD0431, A Phase III Study for the Treatment of Children and Adolescents with Newly Diagnosed Low Risk Hodgkin Disease
Forouhar MA #206097	O	C	AREN03B2, Renal Tumors Classification, Biology, and Banking Study
Forouhar MA #207056	C	C	ACNS0223: A Pilot Study Using Carboplatin, Vincristine, and Temozolomide for Children < 10 Years with Progressive/Symptomatic Low-Grade Gliomas
Forouhar MA #207057	O	M	Safety and Efficacy of Varicella Zoster Immune Globulin (Human) (VariZIG™) in Patients At-Risk of Varicella Infection

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Forouhar MA #207071	O	C	AAML0531; A Phase III Randomized Trial of Gemtuzumab Ozogamicin (Mylotarg®) Combined with Conventional Chemotherapy for De Novo Acute Myeloid Leukemia (AML) in Children, Adolescents, and Young Adults
Forouhar MA #207087	O	C	AREN0532, Treatment for Very Low, Low and Standard Risk Favorable Histology Wilms Tumor
Gries DM #205065	O	L	Staphylococcus Aureus Intestinal Colonization Among Healthy Infants
Hogue JS #207048	O	L	Mupirocin resistance among Staphylococcus aureus isolates at Madigan Army Medical Center
Johnson ER #206021	C	L	EKG Screening in ROTC Cadets; Is It Useful?
Kramer LC #203119	C	L	Alternating Antipyretics: Antipyretic Efficacy Of Acetaminophen Versus Acetaminophen Alternated With Ibuprofen In Children
Lieuw KH #94092	C	C	POG 9351/CCG 7921: Trial of Doxorubicin, Cisplatin, and Methotrexate With and Without Ifosfamide, With and Without Muramyl Tripeptide Phosphatidyl Ethanolamine (MTP-PE) for Treatment of Osteogenic Sarcoma
Lieuw KH #96097	C	C	POG 9440: National Wilms Tumor Study - 5: Therapeutic Trial and Biology Study
Lieuw KH #206051	T	M	ANBL0032 Phase III Randomized Study Of Chimeric Antibody 14.18 (Ch14.18) In High Risk Neuroblastoma Following Myeloablative Therapy And Autologous Stem Cell Rescue
Moffitt DR #204040	O	M	National Cystic Fibrosis Foundation Patient Data Registry
Puntel RA #203046	O	M	Telemedicine Based Ultrasound for Detecting Neonatal Heart Disease in Babies at Remote Military or Native American Health Care Facilities
Puntel RA #204028	E	A	Pediatric Intubation Training Utilizing the Ferret (mustela putorius furo) Model
Puntel RA #207044	O	A	Pediatric Intubation Training Utilizing the Ferret (mustela putorius furo) Model
<b>Department of Preventive Medicine</b>			
Badzik DA #207064	C	L	Hearing Loss in U.S. Army Aviators, Comparing 2005 to 2001
Erickson KE #207033	O	L	Impact of the DoD Paradigm Shift on VA Amputee Care
Sigmon MJ #207026	C	L	Where There's Smoke, is There Disease? A Study of Environmental Airborne Exposures in Soldiers Returning From Iraq
Wiesen AR #205099	C	L	CD4+ T Cell Epitope Identification for Protective Antigen of Bacillus Anthracis
Wiesen AR #207028	O	L	An open-label randomized, controlled pilot study of the tolerability, compliance, and short-term effectiveness of rifampin vs. isoniazid for the treatment of latent tuberculosis infection

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### Department of Psychiatry

Peterson KA #204089	O   M	A Placebo-Controlled Trial of Prazosin vs. Paroxetine in Combat Stress-Induced Nightmares and Sleep Disturbance
Peterson KA #206011	O   M	Prazosin for the Treatment of Trauma Nightmares in PTSD
Peterson KA #207020	O   M	The Impact of Parental Wartime Deployment on Adjustment of Children

### Department of Psychology

Darnell JN #206062	C   L	Military Readiness Risks: Leader Perspectives Impact on Mandatory Addiction Referrals
Gahm GA #207011	O   L	Corresponding Authors' Compliance with E-mail Requests for Additional Information
Gahm GA #207073	O   L	Evaluation of the Post Deployment Health Assessment (PDHA) & Post-Deployment Health Reassessment (PDHRA) Program
Johnson PL #205019	O   L	Theory-Guided Anticipatory Guidance
Reger GM #206118	O   L	User Centered Design Feedback for the Virtual Iraq
Reger MA #206077	O   L	Army Suicide Event Report: Data Analysis
Reger MA #206088	O   L	Exposure to Death and Dying and Mental Health Response in Operation Iraqi Freedom
Steigerwald JR #207114	O   L	Identifying Image Management in Neuropsychological Testing with the CVLT-2, and the Malingering Index and Rogers' Discriminant Function of the PAI in Military Organizations

### Department of Radiology

Balingit AG #202117	O   L	Intravenous Administration of 131 I-6-B Iodomethylnorcholesterol (NP-59) for Adrenal Evaluation and Imaging
Halligan JB #204069	O   S	SWOG RTOG 0212, A Phase II/III Randomized Trial of Two Doses (Phase III-Standard vs. High) and Two High Dose Schedules (Phase II-Once vs Twice Daily) for Delivering Prophylactic Cranial Irradiation for Patients With Limited Disease Small Cell Lung Cancer
Halligan JB #207051	O   S	CTSU RTOG 0521, A Phase III Protocol of Androgen Suppression (AS) and 3DCRT/IMRT vs. AS and 3DCRT/IMRT Followed by Chemotherapy with Docetaxel and Prednisone for Localized, High-Risk Prostate Cancer
Halligan JB #207111	O   M	Reduced PTV Margins for the Treatment of Prostate Cancer with IMRT Using Real-Time, State-of-the-Art Motion Tracking with the Calypso 4D Localization System®: A Feasibility Study
Lewis WT #205024	O   L	Computed Tomography of the Abdomen Following Appendectomy
Park MH #207059	C   L	Retrospective Evaluation of Endovascular Interventions for War Related Extremity Injuries at Madigan Army Medical Center

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Reece WB #206053	T	M	NSABP B-39 / RTOG 0413 A Randomized Phase III Study of Conventional Whole Breast Irradiation (WBI) Versus Partial Breast Irradiation (PBI) for Women with Stage 0, I or II Breast Cancer
Semerad DC #205134	O	L	Clinical Trial and Retrospective Review to Determine the Sensitivity and Specificity of Iminodiacetic Acid Scintigraphy for Fibrolamellar Carcinoma
Semerad DC #207079	O	L	Clinical Trial to Determine the Accuracy of D-Dimer for Resolution of Acute Pulmonary Embolism
Statler JD #205051	C	L	Carotid Stenosis: Digital Subtraction Angiography, Magnetic Resonance Angiography, and the Evolution of Preoperative Evaluation
<b>Special Forces Group, Fort Lewis</b>			
Wendt EP #206018	O	A	1st Special Forces Group (Airborne) Instructing Combat Trauma Management to Trainees
Wendt EP #206106	O	A	1st Special Forces Group (Airborne) Combat Trauma Management Procedures Training for Special Forces Medical Personnel
<b>Cardiothoracic Service, Department of Surgery</b>			
Havenstrite KA #207070	O	M	A Randomized, Double-blind, Placebo-controlled study of Glypromate in Patients Undergoing Cardiopulmonary Bypass Surgery (SNUG-2)
<b>General Surgery Service, Department of Surgery</b>			
Arthurs ZM #203090	C	L	The Association Of Elevated C-Reactive Protein With Presence And Degree Of Carotid Stenosis
Arthurs ZM #206032	C	L	Colonic Ischemia Following Abdominal Aortic Aneurysm Repair-- Open vs. Endovascular Approaches
Arthurs ZM #206123	C	L	Renovascular Hypertension: A Retrospective Analysis of Renal Artery Stenting Outcomes
Arthurs ZM #207007	C	L	Panniculectomy Following Massive Weight Loss After Bariatric Surgery: A Descriptive Analysis
Arthurs ZM #207112	O	L	Technical Success, Conversion, and Complications in Patients Undergoing Totally Percutaneous Aortic Aneurysm Repair With and Without Ultrasound-Guided Access
Arthurs ZM #207113	C	L	Endovascular Aneurysm Repair: The Impact of Transrenal Fixation on Renal Function
Beekley AC #205075	O	L	Operation Iraqi Freedom Combat Trauma Database from the 31st Combat Support Hospital, Baghdad, Iraq
Brounts LR #207009	O	L	Influence of Post-Bariatric Surgery Weight Loss on Endothelial Progenitor Cells, Inflammation, and Oxidative Stress in the Morbidly Obese
Brounts LR #207031	O	L	Prospective Randomized Control Study of Vacuum Assisted Closure Device for therapy in pilonidal disease
Brounts LR #207126	O	L	Influence of Post-Bariatric Surgery Weight Loss on Lower Extremity Vein Hemodynamics

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Brown TA #205112	T	S	RTOG 0412 / SWOG S0332, Phase III Randomized Trial of Preoperative Chemotherapy Versus Preoperative Concurrent Chemotherapy and Thoracic Radiotherapy Followed By Surgical Resection and Consolidation Chemotherapy in Favorable Prognosis Patients with Stage IIIA (N2) Non-Small Cell Lung Cancer
Brown TA #206015	O	M	A Prospective Randomized Study Comparing Sentinel Lymph Node (SLN) Evaluation with Standard Pathological Evaluation for the Staging of Colon Carcinoma
Brown TA #206110	T	A	Comparative Medical/Surgical Research and Development (Limited)
Carter PL #202013	O	L	Bariatric Surgery Effects on the Comorbidities of Obesity
Cronk DR #206040	T	L	Does SDF-1 Production by Atherosclerotic Plaques Correlate with Severity of Carotid Artery Stenosis?
Cuadrado DG #203034	T	L	Impact of Gastric Bypass with Subtotal Gastrectomy on Plasma Ghrelin Profile
Cuadrado DG #206041	C	L	Breast Abscesses Following Nipple Piercing: A Case Series and Review of the Literature
Cuadrado DG #207049	O	L	Is Bariatric Surgery Safe in Patients Over Age 50: A Retrospective Review
Eckert MJ #207045	C	A	Bioprosthetic Repair of Severe Duodenal Injuries in sp. Sus scrofa
Eckert MJ #207046	O	L	Evaluation of the Incidence of Hypovitaminosis and Visual Changes in the Gastric-Bypass Surgery Population
Herbert GS #201020	O	L	Learning Curves for Airway Assessment and Endotracheal Intubation - Cumulative Sum Analysis
Herbert GS #205063	C	L	The Impact of Nodal Micrometastases on Survival of Women with Breast Cancer
Herbert GS #205125	T	L	Prospective, Randomized, Placebo-Controlled Trial of Tegaserod for Treatment of Delayed Gastric Emptying after Pancreaticoduodenectomy
Herbert GS #205126	T	L	Prospective, Randomized, Placebo-Controlled Trial of Tegaserod for Treatment of Post-Operative Ileus Following Partial Colectomy
Herbert GS #206010	T	L	Does Control of Inflammation Prior to Intervention for Carotid Artery Disease or Lower Extremity Peripheral Arterial Disease Affect Outcome?
Herbert GS #206026	C	L	Determination of Telomerase Activity in Atypical Ductal Hyperplasia of the Breast
Herbert GS #206027	O	L	Prognostic Significance of Telomerase Activity in T1 and T2 Rectal Adenocarcinoma for Patients Undergoing Transanal Excision
Hopkinson MO #207037	O	L	The Association of Ethnicity with Presentation and Mortality in Colorectal Cancer
Kjorstad RJ #206043	C	L	Colorectal Complications of External Beam Radiation vs. Brachytherapy for Prostate Cancer
Kozminski MP #207058	O	L	Prevalence and Outcomes of Headache Disorders in Obese Patients Undergoing Gastric Bypass Surgery for Weight Loss

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<u>Prin. Invest.</u> <u>#Protocol No.</u>	<u>S</u>	<u>T</u>	<u>Title</u>
Lehmann RK #204001	O	L	Does Intestinal Fatty Acid Binding Protein Predict Strangulation in Mechanical Small Bowel Obstruction?
Lehmann RK #206115	O	A	Hypoxemic Reperfusion Following Lower Torso Ischemia in sp. <i>Sus scrofa</i>
Lehmann RK #207115	O	L	Madigan Army Medical Center Trauma System Triage Criteria Study
Lehmann RK #207117	O	A	Efficacy of Topical Hemostatic Dressings Following Subclavian Artery Injury in <i>Sus Scrofa</i>
Lesperance KE #205080	O	A	Stem cell engraftment in the lipopolysaccharide mouse ( <i>Mus musculus</i> ) model of acute inflammatory injury
Lesperance KE #206004	O	A	The Evaluation of Telomerase Inhibition in a Colorectal Metastasis Model Using Nude Mice ( <i>Mus musculus</i> )
Lesperance RN #207103	O	L	The Yield of Postoperative Fever Workup in General Surgical Patients
Martin MJ #206079	O	L	The Utility and Impact of Standard Trauma Triage Criteria in the Elderly
Perry JT #206038	T	L	Venous Distensibility Index as a Predictor of Radiocephalic Arteriovenous Fistula Maturation
Perry JT #206061	O	L	Utilization of Genetic Testing and Counseling Among Patients with Hereditary Non-Polyposis Colorectal Cancer
Perry JT #207074	O	L	Proteomic Analysis of Serum and Colonic Biopsy Specimens from Patients with Inflammatory Bowel Disease
Rush RM #204058	E	A	Advanced/Combat Trauma Management Training Using Animal Models (Domestic Goat/ <i>Capra hircus</i> , Pig/ <i>Sus scrofa</i> )
Rush RM #207075	O	A	Advanced/Combat Trauma Management Training Using Animal Models (Domestic Goat/ <i>Capra Hircus</i> , Pig/ <i>Sus Scrofa</i> )
Sebesta JA #206101	O	S	ACOSOG Z6041: A Phase II Trial of Neoadjuvant Chemoradiation and Local Excision for uT2uN0 Rectal Cancer
Sohn VY #206114	C	L	Institutional Accuracy of 11- and 8- Gauge Vacuum-Assisted Core Biopsy of Mammographic Breast Lesions
Sohn VY #206116	C	L	Breast Papillomas in the Era of Stereotactic Core Biopsy
Sohn VY #207018	C	L	Surgical Treatment of Lobular Neoplasia
Sohn VY #207035	C	L	Demographics, Treatment, and Early Outcomes in Penetrating Combat Vascular Trauma
Steele SR #207038	C	L	Laparoscopic vs Open Colectomy for Colon Cancer: Results from a Large Nationwide Population-Based Analysis
<b>Ophthalmology Service, Department of Surgery</b>			
Boden JH #205090	O	L	Attitudes and Perceptions of Refractive Surgery Among ROTC Cadets Presenting for a Flight Physical and Self-Reported Barriers Towards Having Refractive Surgery to Correct Visual Acuity and Becoming Medically Qualified for Army Aviation

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Boden JH #206124	C	L	The use of lidocaine gel prior to povidone - iodine antisepsis and its effect on microbial survivability
Solverson DJ #206006	O	L	Virtual Ophthalmosurgical Simulator as a Valid Training Tool
Torres MF #205083	T	L	Ophthalmic Phentolamine Multiple Dose Clinical Trial

### Orthopedics Service, Department of Surgery

Antosh IJ #206022	O	L	Accuracy of Reduction Utilizing Volar Fixation for Dorsally Displaced Fractures of the Distal Radius
Arrington ED #200125	C	L	Subacromial Injection of Corticosteroids versus Ketoralac for Treatment of Shoulder Impingement Syndrome
Arrington ED #201015	O	B	Biomechanics of Various Coracoclavicular Ligament Reconstruction Techniques
Arrington ED #203036	C	L	Intramedullary Fixation of Displaced Acute Middle One-Third Clavicle Fractures
Arrington ED #204051	O	L	Efficacy of Post-operative Hip Spica Wrap Dressing after Primary Hip Arthroplasty in Preventing Post-operative Wound Complications and Blood Transfusions
Arrington ED #206036	O	L	Return to Full Duty after Anterior Cruciate Ligament Reconstruction in the Military Population
Arrington ED #206037	O	L	A Retrospective Review of Injuries Sustained During Operation Iraqi Freedom and Operation Enduring Freedom Requiring Medical Evacuation to a Tertiary Medical Center
Arrington ED #206085	O	L	Pectoralis Major Repairs in Active Duty Soldiers
Arrington ED #207008	O	L	A Prospective, Randomized Study of Graft Selection in Anterior Cruciate Ligament Reconstruction
Arrington ED #207080	O	M	A Comparison of ORTHOVISC® to Corticosteroid Injection in Shoulder Osteoarthritis
Arrington ED #207095	T	M	Double-Blind, Multicenter Phase 3 Study Comparing the Efficacy and Safety of OMS103HP with Vehicle in Patients Undergoing Allograft ACL Reconstruction (Protocol #C03511)
Arrington ED #207096	T	M	Double-Blind, Multicenter Phase 3 Study Comparing the Efficacy and Safety of OMS103HP with Vehicle in Patients Undergoing Autograft ACL Reconstruction (Protocol #C03512)
Benfanti PL #205300	O	M	Stryker Biotech- OP-1 Bone Morphogenetic Protein, BMP-7 (HUD)
DeVine JG #205053	O	M	A Prospective, Randomized Clinical Investigation of the Cervitech, Inc. Porous Coated Motion Artificial Disc for Stabilization of the Cervical Spine at One Level between C3-C4 and C7-T1
DeVine JG #206081	O	L	Magnetic resonance imaging evaluation of adjacent segments after lumbar disc arthroplasty using the SB Charite implant
Devine JG #206082	O	L	Magnetic Resonance Imaging Evaluation of Adjacent Segments After Cervical Disc Arthroplasty Using the PCM Implant



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<u>Prin. Invest.</u> <u>#Protocol No.</u>	<u>S</u>	<u>T</u>	<u>Title</u>
DeVine JG #206120	O	M	A Single Blind, Multi-Center, Randomized, Prospective Clinical Study Comparing Optecure™ Autograft Extender to Autograft Only in Fusion of the Lumbar Spine
DeVine JG #207053	O	M	A Prospective, Multi-Center Clinical Study to Assess the Safety and Effectiveness of the Impliant TOPST™ System
Ghidella SD #205013	T	M	A Double-blind, Randomized, Placebo-controlled Phase 2b Study to Establish the Effective Dose Range and to Evaluate the Safety of Chrysalin in Adult Subjects with a Fractured Distal Radius
Ghidella SD #206009	O	L	A Randomized Study of Volar Fixed-Angle Plate Fixation Versus Closed Management for Fractures of the Distal Radius
Manoso MW #207052	C	M	A Randomized, Double-blind, Active-And Placebo-Controlled, Parallel Group, Multicenter Study To Evaluate The Efficacy And Safety of Multiple Doses of CG5503 Immediate-Release Formulation In Subjects Awaiting Primary Joint Replacement Surgery for End-Stage Joint Disease
Parada SA #207002	C	L	Functional Outcome in Patients with Post-Operative Infections After Anterior Cruciate Ligament Reconstruction

### Otolaryngology Service, Department of Surgery

Boseley ME #206030	O	A	Pediatric Bronchoesophagology Laboratory using Swine (Sus scrofa)
Chiara JA #205050	O	L	Celecoxib Versus Oxycodone in Uvulopalatopharyngoplasty Surgery: A Comparison of Post-Operative Risks and Benefits
Crawford JV #205052	T	M	MET™ Fully Implantable Ossicular Stimulator Clinical Trial Protocol
Grafenberg MR #205120	O	L	Complications and Audiologic/Tympanometric Findings in Children with Cleft Lip/Palate and Cleft Palate
Poss JM #206020	C	L	Clinical Survey of Community Physicians: Post-Tympanostomy Tube Placement and Swimming Precautions/Treatment Otitis Media with Effusion
Poss JM #206125	O	L	Base of Tongue Reduction for Persistent Obstructive Sleep Apnea Using the Coblator II System: A Pilot Study
Sorensen DM #204070	C	L	Perioperative Immunonutrition in Head and Neck Cancer
Spear SA #206057	C	L	Review of Thyroid Cancer Treatment Outcomes at a Major Medical Center from 1996-2000
Wilhelm MJ #205009	O	L	Inferior Turbinate Reduction Comparing Turbinate Microdebrider, Coblation and Bipolar Cautery

### Urology Service, Department of Surgery

Baker KC #201107	C	M	A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of 10 mg Atrasentan in Men with Metastatic, Hormone-Refractory Prostate Cancer (M00-211)
Baker KC #201113	T	M	A Phase III, Extension Study to Evaluate the Safety of 10 mg Atrasentan in Men with Hormone-Refractory Prostate Cancer (M00-258)

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<u>Prin. Invest.</u> <u>#Protocol No.</u>	<u>S</u>	<u>T</u>	<u>Title</u>
Baker KC #201121	C	M	A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of 10 mg Atrasentan in Men with Non-Metastatic, Hormone-Refractory Prostate Cancer (M00-244)
Baker KC #203035	O	M	A Multi-Institutional Pilot Study to Evaluate Molecular Markers in Urine and Serum in the Early Detection of Prostate Cancer
Baker KC #204005	O	M	A Phase III, Randomized, Double-Blind, Placebo-Controlled Trial Evaluating the Ability of Risedronate to Prevent Skeletal Related Events in Patients with Metastatic Prostate Cancer Commencing Hormonal Therapy, Protocol #GU02-41
Baker KC #204091	O	M	A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate AMG 162 in the Treatment of Bone Loss in Subjects Undergoing Androgen-Deprivation Therapy for Non-Metastatic Prostate Cancer
Baker KC #204120	O	L	The Effect of Flexible Cystoscopy on the Serum PSA Values
Baker KC #205006	O	M	A Randomized, Double-Blind, Placebo-Controlled, Multicenter Efficacy and Safety Study of Toremifene Citrate for the Prevention of Bone Fractures in Men with Prostate Cancer on Androgen Deprivation Therapy (Protocol #G300203)
Baker KC #205017	C	A	Madigan Army Medical Center Advanced Laparoscopic Training Using the Pig (Sus scrofa)
Baker KC #205040	C	L	The Epidemiology of Nephrolithiasis in Soldiers Returning From Operation Iraqi Freedom
Baker KC #205092	C	M	A Multi-center, Randomized Clinical Investigation of Trelstar™ Versus Continued Therapy in Patients Receiving Lupron or Zoladex for Advanced Prostate Cancer
Baker KC #205119	O	L	Expression of CXCR4 in Archived Prostate Cancer Specimens and its Association with Patient Demographics, Pathologic Results, and Outcomes
Baker KC #206039	C	M	SEER Rapid Response Surveillance Study #5, Prostate Cancer Therapy Selection (PCATS) Study
Baker KC #206072	C	M	A Randomized, Double-Blind, Placebo-Controlled, Multi-Center Phase 3 Study of Denosumab on Prolonging Bone Metastasis-Free Survival in Men with Hormone-Refractory Prostate Cancer
Baker KC #206100	C	M	A Randomized, Double-Blind, Multicenter Study of Denosumab Compared with Zoledronic Acid (Zometa®) in the Treatment of Bone Metastases in Men with Hormone-Refractory Prostate Cancer (20050103)
Brand TC #204079	O	M	Uniformed Services University Multi-Center National Database for the Center for Prostate Disease Research (CPDR) with Patterns of care, Outcomes, and Prognostic Analyses
DeCastro BJ #202065	C	M	Oral Ketoconazole For Prevention Of Postoperative Penile Erection, A Prospective, Randomized, Double Blind Trial
Gurski JL #205136	O	L	The Incidence of Infection and Stent Colonization in Patients With and Without Strings
Gurski JL #207014	O	L	Postpartum Durabilities of Anti-Incontinence Surgery in Women of Child-Bearing Age

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<u>Prin. Invest.</u> <u>#Protocol No.</u>	<u>S</u>	<u>T</u>	<u>Title</u>
Nelson DM #205076	O	L	Madigan Army Medical Center's Current Clinical Practice and Experience With Osteopenia And Fractures In Men Treated With Androgen Deprivation Therapy
Peterson AC #202122	O	L	Followup of Testicular Microlithiasis in an Asymptomatic Population
Peterson AC #203042	O	M	A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study of the Efficacy and Safety of Dutasteride 0.5 mg Administered Orally Once Daily for Four Years to Reduce the Risk of Biopsy-Detectable Prostate Cancer, Protocol Number ARI40006
Peterson AC #203081	C	M	Study of the Safety and Effectiveness of the Mentor Two-Piece Inflatable Penile Prosthesis, Protocol Number U108-802-4
Peterson AC #204032	C	M	Prospective, Observational Registry and Patient Survey of the Management of Men with Symptomatic Benign Prostatic Hyperplasia (BPH): BPH Registry and Patient Survey Protocol #L8890
Peterson AC #204078	C	M	Long-Term Open-Label Extension Trial for Subjects Completing the Phase 3 Trial of Fesoterodine (SP584) for the Treatment of Overactive Bladder Syndrome
Peterson AC #204086	C	M	Prospective, Open-Label, Non-Comparative, Multi-Center Study to Evaluate the Efficacy and Safety of Ciprofloxacin Extended-Release (Cipro-XR) 1000 mg Tablets Given Once Daily for 7 to 14 Days in the Treatment of Patients 18 Years or Older with Complicated Urinary Tract Infections Caused by Pseudomonas Aeruginosa and Other Common Uropathogens
Peterson AC #205027	O	M	A Randomized, Double-Blind, Placebo-Controlled, Multicenter Efficacy and Safety Study of Toremifene Citrate for the Prevention of Prostate Cancer in Men with High Grade Prostatic Intraepithelial Neoplasia (PIN)
Peterson AC #205073	C	M	A Phase 2, Randomized, Multicenter, Placebo-Controlled, Double-Blind Dose-Ranging Clinical Trial to Study the Efficacy and Safety of 5, 15, or 25 mg/day of CyPat™ (Cyproterone Acetate) for the Treatment of Hot Flashes following Surgical or Medical Castration of Prostate Cancer Patients, Protocol #DR-PCA-201
Peterson AC #205079	O	A	Microsurgery Training Utilizing The Rat (rattus norvegicus) as a Teaching Model
Peterson AC #205135	O	L	Acute Urinary Retention and the Role of Fill and Pull Voiding Trials
Peterson AC #206031	O	L	Adult Circumcision: Template vs Standard Sleeve Technique
Peterson AC #206102	C	M	Phase 2 multicentre, randomised, double-blind, placebo-controlled, pilot study to determine proof of efficacy, safety, tolerability and pharmacokinetics of intravesical PSD597 in the symptomatic management of interstitial cystitis/ Painful bladder syndrome (IC/PBS)
Peterson AC #206117	O	L	Comparison of Non-Contrast Abdominal Computed Tomography (CT) to Contrast CT, Intravenous Pyelography (IVP) and Nuclear Renal Scan for Determination of Renal Function: A Retrospective Review
Pugliese JM #205088	T	L	The Value of Resistive Index: A Longitudinal Study of Confounding Variables and Their Impact - A Pilot Study

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<u>Prin. Invest.</u> <u>#Protocol No.</u>	<u>S</u>	<u>T</u>	<u>Title</u>
Pugliese JM #207005	O	L	The Identification of Seminal Plasma Protein Biomarkers in Patients Presenting with Infertility, Hydrocele, Varicocele, Spermatocele and Testicular Masses
Pugliese JM #207065	O	L	The Role of Extended Meatoplasty in the Management of Urethral Stricture Disease Due to Lichen Sclerosus
<b>Vascular Surgery, Department of Surgery</b>			
Andersen CA #202086	O	M	A Randomized, Controlled Multicenter Trial of Vacuum Assisted Closure Therapy™ in the Treatment and Blinded Evaluation of Diabetic Foot Ulcers (Protocol VAC2001-08)
Andersen CA #203055	C	M	A Randomized, Controlled, Multicenter Trial of Vacuum Assisted Closure Therapy™ in the Treatment and Blinded Evaluation of Pressure Ulcers, Protocol Number VAC2001-01
Andersen CA #205010	C	M	Linezolid In The Treatment Of Subjects With Complicated Skin And Soft Tissue Infections Proven To Be Due To Methicillin-Resistant Staphylococcus Aureus
Andersen CA #205091	O	L	The Prevalence and Progression of Carotid Artery Stenosis in Patients Undergoing Radiation for Head and Neck Cancer
Andersen CA #206012	T	M	A Comparative Prospective, Randomized, Double-Masked, Parallel Group, Sham-Controlled Trial of MIST Therapy for the Reduction of Pain in Chronic Lower Extremity Ulcers
Andersen CA #206071	C	M	Phase 3, Multicenter, Multi-National, Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Efficacy and Safety of Alfimeprase in Subjects with Acute Peripheral Artery Occlusion (NAPA-3)
Andersen CA #206094	C	M	A Multi-Center, Double-Blind, Randomized, Parallel, Vehicle-and Standard Care-Controlled, Dose-Ranging Study Assessing the Safety and Efficacy of MRE0094 Gel When Applied Topically for 90 Days to Subjects with Diabetic, Neuropathic, Foot Ulcers
Andersen CA #207105	O	M	A Prospective, Multi-Centre, Double Blind Randomized Placebo Controlled Clinical Trial To Evaluate The Safety And Efficacy Of ICXP007 In A Phase III Trial With Four-Layer Therapeutic Compression, For The treatment Of Non-Infected Skin Leg Ulcers, Due To Venous-Insufficiency (02-VLU-003)
Roukis TS #206111	C	M	Pivotal Study to Evaluate the Efficacy and Safety of Dermal - Living Skin Replacement (Dermal - LSR) in the Treatment of Chronic Diabetic Foot Ulcers
Roukis TS #206127	O	M	A phase 2B long-term, randomized, open-label, safety and tolerability trial comparing [S,S]-Reboxetine (PNU-165442G) with routine care in patients with chronic painful diabetic peripheral neuropathy (DPN) Study Number A6061031
Roukis TS #207022	O	L	A Prospective, Randomized, Double-Blind, 2-Part Comparative Study of the Effects of Autologous Platelet-Poor Plasma and Oxidized Regenerated Cellulose on the Healing Rates and Pain Reduction of Split-Thickness Skin Graft Harvest Sites, Combined with the Effects of Autologous Platelet Rich Plasma with Topical Negative Pressure and Topical Negative Pressure Alone on the Healing Rates of Split-Thickness Skin Graft Application Sites

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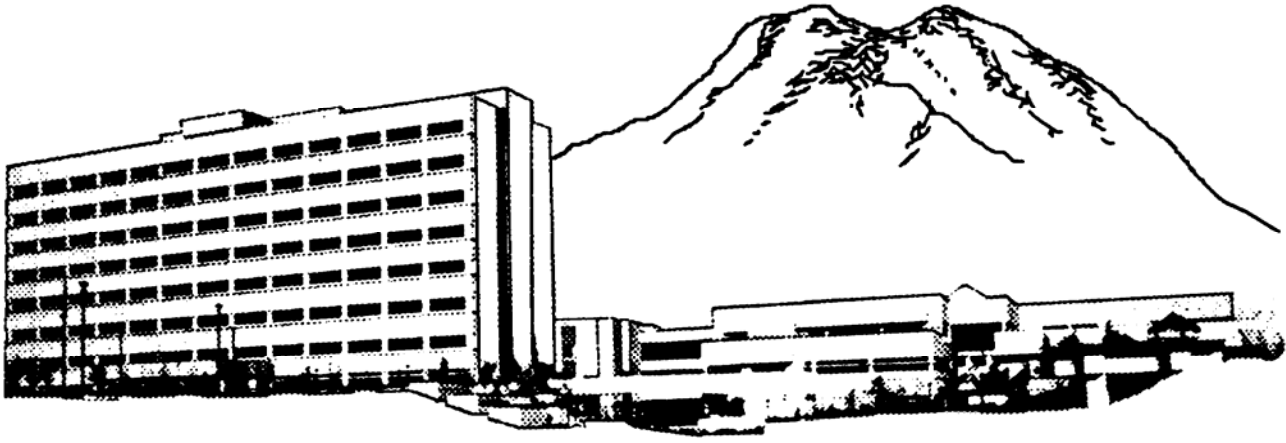
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Prin. Invest.                      S   T   Title

#Protocol No.

Roukis TS #207029	O	L	A prospective, randomized, single-blind comparison of percutaneous tendo-Achilles lengthening and endoscopic Gastrocnemius recession in diabetic patients undergoing a transmetatarsal amputation with peroneal tendon transfer
Schweinberger MH #207082	O	L	Bacterial Skin Contamination Prior To and After Surgical Preparation of the Foot, Ankle, and Lower Leg in Patients with Diabetes and Intact Skin versus Patients with Diabetes and Ulceration: A Prospective Controlled Therapeutic Study
Singh NN #206070	C	M	A Two-Part, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Study to Evaluate the Effect of Simvastatin, Losartan, and Pioglitazone on Cardiovascular Disease Biomarkers in Lower Extremity Atherosclerotic Plaque Excised from Patients with Peripheral Arterial Disease
Singh NN #207010	O	M	Plaque Removal versus Open Bypass Surgery For Critical Limb Ischemia



## **Detail Summary Sheets**

Department of Clinical Investigation

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206122	<b>Status:</b> Ongoing
<b>Title:</b> Profiling of Proteins Extracted from Tissue Taken from Regenerating and Intact Notophthalmus viridescens Limbs Using SELDI		
<b>Principal Investigator:</b> Jeff M. Bullock, M.S.		
<b>Department:</b> Clinical Investigation		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Matthew J. Martin, MC		
<b>Start - Completion:</b> 13 Sep 2006 - Sep 2009	<b>Funding:</b> DCI	<b>Periodic Review:</b> 12 Sep 2007

**Study Objective:** The primary objective is to produce a series of protein profiles from regenerating and non-regenerating limb tissue. Protein profiles for each sample will be compared. Differences in the profiles will be suggestive for which proteins may be involved in tissue regeneration. Candidate proteins will be targeted for further research.

**Technical Approach:** Experimental arms will consist of the following: 1) Amputation followed by enervation at various time points 5, 15, and 30 minutes and 1, 6, and 20-24 hours and 2, 3, 4, 5, and 6 days. 2) Enervation only. 3) Neural transection followed immediately by amputation, followed by blastectomy. Blastectomies will be performed when the blastemas reach the early to mid-late bud stage, but before the pallet stage. 4) Amputation followed by blastectomy. Blastectomies will be performed when the blastemas reach the early to mid-late bud stage, but before the pallet stage. 5) Normal non-regenerating tissue taken from amputated limbs at time of amputation.

For all operations animals will be anesthetized by soaking in a cold (4-10 C) neutralized solution (pH 7.2 - 7.4) of 0.1% w/v Ethyl 3-aminobenzoate, methanesulfonic acid salt (MS222). Forelimbs will be amputated at the mid humerus or mid radius; ulna region and protruding bones trimmed using iridectomy scissors or a suitable analog. Amputation of the first forelimb will be followed immediately by the amputation of the opposite forelimb. Amputated limbs to be saved will immediately be put into cryogenic tubes and snap frozen in liquid nitrogen. Amputees while still anesthetized will be given 100 l of Buprenex by IP injection at a dose of (0.01-0.03 mg/kg) diluted to a concentration of  $3 \times 10^{-4}$  mg/ml with a lactate ringer solution adjusted to a mOsmol/L of 225 +/- 5 using a 5/8 inch 26 gauge needle. Following the Buprenex injection animals are placed on an ice pack covered with a paper cloth for 15-30 minutes before allowing them to warm and placed back into an aquarium. Nerves 3, 4, and 5 of the brachial plexus are the main nervous supply in the newt forelimb. In animals to be enervated these nerves will be removed by excision. Using the tip of a 5/8 inch 26 gauge needle an incision will be made on the ventral side of the forelimb that runs along the entire length of the limbs' proximal distal axis. The epidermis and surrounding muscle are pulled aside to expose the nerves and the rounded bore of the needle is inserted beneath the nerve bundles and pulled along the length of the nerve to free it from any connective tissue. Once the nerve has been exposed and freed it is excised using iridectomy scissors or a suitable analog. Excised nerves to be saved are immediately put into cryogenic tubes and snap frozen in liquid nitrogen. In some cases nerves 3, 4, and 5 will not be removed, but will instead be transected at the brachial plexus. A small incision at the brachial plexus will be made with the tip of a 5/8 inch 26 gauge needle and the nerves severed with iridectomy scissors or a suitable analog. Animals whose nerves were removed or transected while still anesthetized will be given 100 l of Buprenex by IP injection at a dose of (0.01-0.03 mg/kg) diluted to a concentration of  $3 \times 10^{-4}$  mg/ml with a lactate ringer solution adjusted to a mOsmol/L of 225 +/- 5 using a 5/8 inch 26 gauge needle. Following the Buprenex injection animals are placed on an ice pack covered with a paper cloth for 15-30 minutes before allowing them to warm and placed back into an aquarium. If necessary, as determined by the staff veterinarian, a second and third dose of Buprenex will be give at 20-25 hours post-op, and at 46-48 hours post-op. If possible these injections will be given without

anesthesia. In all cases (amputations, enervation, and nerve transections) if Buprenex fails to provide adequate pain relief (as determined by the staff veterinarian) we plan to try other post-op analgesics. Possible choices include: Butorphanol at 0.2-0.4 mg/kg by IP injection, 2% Lidocaine or Bupivacaine administered topically 3-6 hours post-op then as necessary for 24-48 hours. All post-op analgesic care decisions/changes will be at the discretion of the staff veterinarian. Blastemas are removed by transecting the blastemas at the amputation plane using iridectomy scissors or a suitable analog. Once the blastemas have been removed they are immediately put into cryogenic tubes and snap frozen in liquid nitrogen. Following blastema removal animals are placed on an ice pack covered with a paper cloth for 15-30 minutes before allowing them to warm and placed back into an aquarium. No post-op analgesics will be given after removal of blastemas. Depending on the experimental arm an animal is placed in it may under go multiple surgical procedures. However, once an animal has been used in one experimental arm it will not be used in a different experimental arm or reused in the same experimental arm. Animals that have reached the end point of an experimental arm will be euthanized as described below. Animals to be euthanized will be placed in a 0.1 to 1.0 % w/v buffered solution (pH 7.2-7.6) of MS222 for 15-30 minutes until completely sedated. Dose and length of time of MS222 exposure will be at the discretion of the staff veterinarian. Following sedation animals will be decapitated using iridectomy scissors or a suitable analog. All tissues including euthanized animals will be place in the hospital trash for disposal. Tissue to be saved will be snap frozen immediately upon removal. Proteins will be extracted from frozen tissue by sonication and maceration in a buffered lysis solution containing protease inhibitors. Cellular debris will be removed by centrifugation and protein concentration determined by colorimetric spectroscopy. Protein profiles will be done using SELDI. Protein profiles from regenerating blastema and non-regenerating limb tissue along with nerve tissue from regenerating and non-regenerating limbs will be compared. Differences in the profiles will be suggestive for which proteins may be involved in tissue regeneration. Candidate proteins will be targeted for further research.

**Progress:** This protocol received initial approval during a convened meeting of the IACUC on 13 September 2006. Work under this protocol was initiated during FY07, and will continue through FY08. Preliminary results are not yet available.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204100	<b>Status:</b> Terminated
<b>Title:</b> Human Blood Collection for Bench Research Initiatives		
<b>Principal Investigator:</b> CPT Michael J. Hartenstine, MS		
<b>Department:</b> Clinical Investigation		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Daniel G. Cuadrado, MC; MAJ Daniel R. Cronk, MC; CPT Patrick M. McNutt, MS; MAJ Garth S. Herbert, MC		
<b>Start - Completion:</b> 16 Jul 2004 - Jul 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 27 Jun 2006

**Study Objective:** To obtain blood samples from normal, healthy subjects for use in bench experiments involving the behavior of blood cells in culture. To obtain blood samples from normal, healthy subjects for use as controls in bench experiments (e.g., ELISA analyses).

**Technical Approach:** Prospective collection of tissue samples with subjects selected by announcements asking for volunteers at meetings within DCI and DOS. Blood will be aseptically obtained in an amount not to exceed 550ml from any one subject in any 8-week period. Not more than two blood draws will be performed on any one subject in any one week period. Blood will either be used immediately for bench experiments, or frozen and stored for use at a later date. Samples will be de-linked from subjects at the time of blood draw. No additional information will be obtained from subjects. Samples will not be transported out of the DCI. Samples will be destroyed within one year of collection.

**Progress:** This protocol was terminated in June 2007, when it was determined to no longer be useful in obtaining blood samples. Only one subject enrolled in the past three years.

### Detail Summary Sheet

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<b>Date:</b> 30 Sep 07	<b>Number:</b> 205031	<b>Status:</b> Ongoing
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**Title:** Proteomic Analysis of Longitudinally-Collected Maternal Plasma Samples: Establishing the 'Pregnancy Proteome'

**Principal Investigator:** CPT Michael J. Hartenstine, MS

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**Department:** Clinical Investigation

**Facility:** MAMC

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**Associate Investigator(s):** COL Peter G. Napolitano, MC; MAJ Garth S. Herbert, MC; Danielle L. Ippolito, PhD; MAJ Jennifer L. Gotkin, MC; CPT Daniel G. Cuadrado, MC; CPT Patrick M. McNutt, MS; CPT Jeremy P. Cerver, MS; Heidi M. Cederholm, B.S.; Aspen M. Bergmann, B.S.; COL Jerome B. Myers, MC

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**Start - Completion:**  
23 Mar 2005 - May 2006

**Funding:**  
DCI

**Periodic Review:**  
10 Jan 2008

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**Study Objective:** To determine the baseline proteome for a normal pregnancy and assess the changes in protein among maternal plasma samples.

**Technical Approach:** Investigators propose to collect samples at the first OB/GYN physician visit ( NLT 12 weeks), during the second trimester analyte screen (~16-22weeks), early third trimester (26-28weeks), late third trimester (~36-38 weeks), upon admission for labor and at 6-10\* weeks post-partum, as well as cord blood collected at delivery. Plasma will be longitudinally collected from 300 pregnant women to conduct a pilot analysis of 10 representative patients with uncomplicated pregnancies at 3 time points. The preliminary results will be used for an initial publication and to pursue more substantive funding for a detailed analysis. The samples will be available for collaboration with other researchers under the auspices of the IRB, and under the direction of the research operations service component of DCI.

**Progress:** As of January 2007, a total of 129 subjects enrolled in this study at MAMC, 95 in the last 12 months. Significant improvement in subject enrollment has been achieved. Crude samples of 15 women have been profiled, which yielded the beginnings of a proteomic fingerprint of pregnancy. In addition to profiling samples from uncomplicated pregnancies, several miscarriage samples have been profiled and two specific proteins have been observed to be elevated in miscarriage samples. Pooled samples are also being analyzed to determine proteins changing in all subjects as a function of gestation. Several peaks have been identified as predictive of gestational age. The collection of clinical data has begun on the subject population in order to better characterize the samples in the tissue bank.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205044	<b>Status:</b> Terminated
<b>Title:</b> A Prospective Study of Pseudocholinesterase Activity in Patients with Fibromyalgia, Chronic Pain, Pelvic Pain and Hernias		
<b>Principal Investigator:</b> CPT Michael J. Hartenstine, MS		
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Patrick M. McNutt, MS; CPT Daniel G. Cuadrado, MC; CPT Kathleen M. Goings, MC; CPT Jeremy P. Cerver, MS; MAJ Brian T. McKinley, MC; CPT Kyle C. Harner, MC; CPT Christopher S. Murphy, MC		
<b>Start - Completion:</b> 17 Mar 2005 - Nov 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 22 Feb 2006

**Study Objective:** To determine if there is a correlation between levels of serum cholinesterase and acute and chronic pain.

**Technical Approach:** Five separate groups will be analyzed for this protocol. Group 1, hernia surgery, patients identified with an inguinal hernia who are scheduled for surgery with the Department of General Surgery will be enrolled following detailed pre-operative history and physical examination and standard pre-operative laboratory evaluation. Those enrolled in the study will fill out a questionnaire at the time of this appointment and be consented by a member of the study staff or resident. During their routine pre-operative blood draw an additional 3cc purple top tube will be collected and sent to DCI. There the specimen will be centrifuged and the serum will be collected and snap frozen for analysis.

Immediately post-operatively, while in the recovery room, a second blood draw will be performed and the sample likewise sent to DCI for processing. A third and final 3cc specimen will be collected at the two week routine follow-up appointment at which time a second questionnaire will be completed. Group 2-4, Chronic pain, Fibromyalgia and Pelvic pain, patients will be identified at the Anesthesia pain, Rheumatology and Gynecology clinic for eligibility for entry in the study protocol. Those who meet criteria will complete the study questionnaire and undergo a single 3cc blood draw. The blood will be collected in a 3cc purple top tube and transported to DCI for processing. Samples will be labeled with a patient number and diagnosis. Group 5, Normal controls, twenty normal control patients will fill out the study questionnaire and have a single blood draw. The specimen will be collected in a 3cc purple top blood and processed in DCI.

Sample handling and determination of PCE activity: Samples will be collected, processed, aliquoted in 100uL fractions and stored at -70°C in DCI. SchEs are extremely stable molecules so short periods (<12hrs) between collection and processing should not interfere with measurements of enzyme activity. 20.0uL of serum are added to 40.0uL of a 25% sucrose solution containing 10mM Tris-formate (pH 9.0). 3.0uL are then separated by vertical flat bed polyacrylamide gel electrophoresis on a 6.5% T: 5.0% C gel using a borate-sulfate discontinuous buffer system. Following electrophoresis, the gel is equilibrated in 96mL Tris-chloride (pH 6.6) in the presence of FAST Red TR or Fast BLUE RR as the diazonium salt for five minutes with gentle agitation. Add 4.0mL of 1.0% sodium alpha naphthyl acetate in acetone solution (the substrate) and allow the reaction to proceed for ten minutes at room temperature with constant agitation. Stop the reaction with 10% acetic acid. The resulting insoluble diazonium complex bands mark esterase activity. Quantify the esterase activity by quantitative densitometry. Densitometric results are presented as the integrated area under the curve of each peak expressed in pixels. The bench researcher will have access to patient numbers only and will be unaware of the diagnosis. Results will be tabulated in a password protected spreadsheet for statistical analysis after completion of specimen collection.

**Progress:** This protocol was terminated due to lack of institutional interest in FY07, with 31 of the required 220 subjects providing serum for this bench protocol. Results of the tests run on these samples was provided by Dr. Robert Allen.

**RESULTS:** Based on visual assessment scores of how much pain a person had on a scale of 1-10, with a score of 10 being the most severe, data between the two studies are similar with a significant increase in psuedocholinesterase amount as the VAS increases to levels of 7 or above. Esterase levels for 4 groups of VAS scores: VAS 0, 2797 (n=24); VAS 5-6, 3457 (n=4); VAS 7, 3544 (n=3); VAS 8, 4445 (n=3). Psuedocholinesterase levels for 4 groups of VAS scores: VAS 0, 3194 (n=22); VAS 7, 4436 (n=35); VAS 8, 4627 (n=23); VAS 10, 4739 (n=15).

**DISCUSSION:** While the initial protocol called for serum collection, in actuality plasma was collected, which led to several samples being discarded due to nonresolvable cryoprecipitate, and the 100 patients that were specified in the protocol in five groups of 20 were not realized. The patients own assessment of pain level has limitations in self-assessing each may have a different perception of how severe his or her pain is , for example, one patient with a self-assessed level of 6 had an esterase level similar to the VAS 8 group. On the other hand, a previous study detected an individual fraudulently drawing workman's compensation with supposed back pain with a normal esterase level. One volunteer with fibromyalgia showed no increase in psuedocholinesterase amount, and in fact was on the low end of the normal value. No opportunity to study acute pain other than a tonsillectomy patient with samples obtained before and during the acute throat pain phase show no difference in amount, and was actually lower on a paired sample in comparison to one taken during the pain episode. Thus, no acute pain data were available from this study, nor was phantom pain associated with amputation.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206091	<b>Status:</b> Ongoing
<b>Title:</b> MAMC Rodent and Rabbit Quality Assurance and Sentinel Program		
<b>Principal Investigator:</b> MAJ Nancy L Merrill, VC		
<b>Department:</b> Clinical Investigation		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.; MSG Karen L Van Loon, USA; SGT Anita J. Teadt, USA; SPC Miemie T. Phillips, USA; SPC Shayla M. Phyll, USA; Shelley L. Spahn-Bridges; Jennifer L. Theis		
<b>Start - Completion:</b> 10 May 2006 - May 2009	<b>Funding:</b> DCI	<b>Periodic Review:</b> 17 May 2007

**Study Objective:** The purpose of this protocol is to provide a reliable program for preventing the introduction of adventitious organisms into the MAMC rodent and rabbit colonies. This will be accomplished by sampling species from selected sources as they are received into the facility. Suspect groups of animals will be quarantined based on vendor health reports, and their release from quarantine will depend on results of quality assurance tests. Continuous health monitoring or surveillance will be accomplished by housing sentinel animals in the animal rooms, and then periodically submitting them for quality assurance testing.

**Technical Approach:** Experiment 1: Sentinel Surveillance: Sentinel animals must be of known health status as indicated below in para. V.3.3.7. For this purpose, sentinel mice will be purchased from JAX or Harlan and sentinel rats from JAX or Harlan. Sentinels will be kept in the colony at least one month before they are sacrificed and tested, allowing for any potential exposures and subsequent seroconversion to occur. Complete procedural techniques are outlined in LARS Quality Assurance of Rabbits and Rodents and Sentinel Surveillance SOPs.

a. Mice: A minimum of 16 mice, 4 cages of 4 mice per cage, will be placed in each occupied mouse room initially (preferably at the beginning of the calendar year). During cage changing soiled bedding will be collected from at least 2-3 cages off of each rack in the room and placed in a clean container and well mixed. The sentinel animals will be changed last. A handful of the mixed dirty bedding will be broadcast over the clean bedding of a fresh cage before adding the sentinel animals to the cage. Sentinel cages will be unfiltered, as open to the room as possible. One cage of mice will be sacrificed each quarter. At the mid-point of the quarter, 2 of 4 mice in the cage will be sacrificed for serology screening. The blood will be pooled from those 2 animals and sent to Research Animal Diagnostic Laboratory (RADIL), University of Missouri. At the end of the quarter, the remaining 2 mice will be sacrificed for comprehensive testing to include serology and pathology by RADIL and in-house parasitology (including examination of pelts for external parasites). Feces from each room will be pooled every six weeks and submitted for Helicobacter testing by RADIL.

1) Should any rooms be used for breeding, sentinel mice will be selected from the indigenous population. Retired breeders will be used for serology, whereas parasitology and pathology will be performed on weanlings and young adults.

2) Extra animals (2 per 16 animals) will be ordered with each sentinel purchase, if not from JAX or Harlan. See section V.1.2 These animals will be sacrificed within one day of delivery and submitted for Quality Assurance Procedures described in para. V.4.4.2.

b. Rats: Sentinel rats will be managed in a similar manner, except they may be housed singly. For long-term housing of rats (greater than two months), two sentinel rats will be added to each occupied rat room initially. The cages will contain a sample of soiled bedding from each rack of animals in the room each time the cages are changed, similar to the procedures for changing mice. At the mid-point of the quarter 1 rat will be sacrificed for serology and parasitology, and 1 rat will be sacrificed for a comprehensive pathologic examination, serology and parasitology at the end of the quarter. Feces from each room will be pooled every six weeks for floatation and testing for Helicobacter. One additional rat will be ordered with each sentinel rat

purchase. This animal will be sacrificed within one day of delivery and submitted for Quality Assurance Procedures described in V.4.4.2.

c. In the face of a potential infectious disease outbreak, these sampling timetables are compressed under the direction of the Chief, Laboratory Animal Resources Service, and are based on pathogenesis of the suspected agents.

**Experiment 2: Quality Assurance Sampling:** For the approved vendors (Harlan and Jackson Labs), the Chief, LARS will review and sign diagnostic health reports for the incoming shipment to ensure that the incoming animals are free of adventitious organisms. These reports must be current within six months. For other vendors, quality assurance will be performed on animals from the same barrier and/or species/strain as those ordered.

In the event that animals from any approved vendors are found to be the source of an adventitious organism within the animal colony, two extra mice/rats will be ordered with each shipment and processed for QA testing until it is determined that additional testing is no longer necessary. This determination will be based upon a current literature review of the epidemiology and pathophysiology of the individual organism(s) in question.

If rodents or rabbits are received from an unknown vendor, they must have a diagnostic health report current within six months. For these unknown vendors, additional animals (a minimum of 3-5%, but not less than two animals, at the discretion of the Chief, LARS, of the same strain, facility, and barrier/location will be ordered with each shipment and will be submitted for quality assurance testing. The Chief, LARS will base his/her decision upon a current literature review of the epidemiology and pathophysiology of the individual organism(s) in question and upon current quality assurance standards within the industry.

**Data Analysis:** Statistical analysis will not be necessary in this protocol. Results of serology, parasitology, and pathologic examination will be used to determine whether or not adventitious organisms enter the animal colony, their spread, and whether control measures are effective in preventing and eliminating these agents.

**Progress:** This protocol used eight animals in two rooms. Submitted samples identified a newly characterized murine norovirus from that particular vendor. In the future, a new vendor will be used that screens for the particular virus. This will maintain our infectious disease surveillance and quality control in our animal colonies.

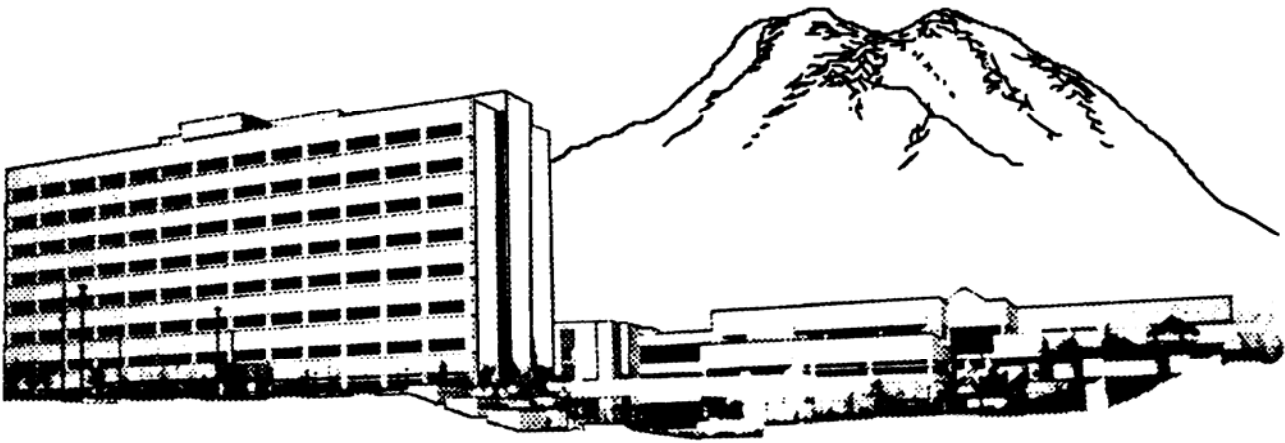
### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206109	<b>Status:</b> Ongoing
<b>Title:</b> Animal Tissue Use in Biomedical Research and Training		
<b>Principal Investigator:</b> MAJ Nancy L Merrill, VC		
<b>Department:</b> Clinical Investigation		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Joren B. Keylock, MC; James R. Wright, BA, MT (ASCP); Donna J. Frey; CPT Matthew J. Eckert, MC		
<b>Start - Completion:</b> 12 Jul 2006 – Jul 2009	<b>Funding:</b> Verus Pharmaceuticals via DCI	<b>Periodic Review:</b> 30 May 2007

**Study Objective:** To reduce live animal use in biomedical research or training at MAMC by facilitating animal tissue use as alternative research/training models, where feasible. Objectives for individual projects proposed under this protocol will be defined in project addendum.

**Technical Approach:** In the past, personnel requesting authorization to conduct biomedical research or training using postmortem animal tissues have been required by the MAMC IACUC to submit a "stand alone" animal care and use protocol that describes the proposed tissue use, background, justification, animal care provisions, literature searched conducted all in accordance with federal animal welfare regulations. Many of the provisions and assurances contained in the DoD-mandated animal use protocol format did not apply to research or training activities using animal tissues only. The task of preparing full protocols and related animal use reports for such activities places an unnecessary burden on individuals wishing to reduce live animal use by justifiable utilization of animal tissues. The "alternative" use of postmortem animal tissues rather than live animals (Reduction or Replacement) can be significantly facilitated by streamlining the preparation, submission, tracking and reporting of such research or training activities under an umbrella or stand protocol that spells out universal conditions for animal tissue use and identifies a Principal Investigator (PI) who is responsible for overseeing these activities.

**Progress:** This protocol supported five suture training labs for 45 medical personnel and three research labs to further characterize the physical effects of Epi-Pens. This protocol obtained tissue samples from protocols #206078, 205017, and 206115. This tissue sharing minimizes the use of live animals.



# Detail Summary Sheets

## Hospital Dental Clinic



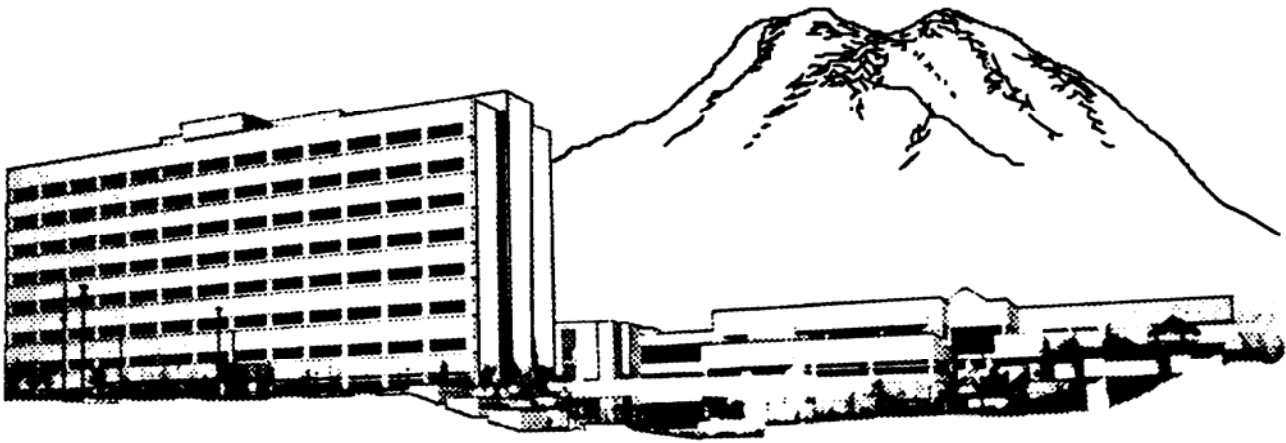
### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203116	<b>Status:</b> Terminated
<b>Title:</b> Host Response Gene 203014 in Military Populations		
<b>Principal Investigator:</b> MAJ Scott W. Burgan, DC		
<b>Department:</b> Dentistry		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Paul O. Francis, DC; Richard P. Darveau, Ph.D.; MAJ Douglas R. Dixon, D.M.D., M.S.D; COL (Ret) Robert B. O'Neal, DMD, MEd, MS; LTC Edward B. Fowler, DC; Frank A. Roberts, D.D.S., Ph.D.; Beverly Dale, Ph.D.		
<b>Start - Completion:</b> 12 Sep 2003 - Sep 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 29 Aug 2006

**Study Objective:** To determine the incidence of polymorphisms (mutations) in bacterial receptors between periodontitis-affected and periodontally healthy dental patients.

**Technical Approach:** This study will look at a single nucleotide polymorphisms (SNP's) found in hTLR and other host response genes that will be examined for their association with periodontitis in the Hispanic and African American military population. Approximately 450 patients will be enrolled in this study here at MAMC 225 periodontically healthy and 225 periodontitis-affected that are 18 years of age and older. The frequency of different TLR pleomorphisms found in the populations will be determined for their association to periodontitis using genomic DNA isolated from cheek swab samples and compared for binomial proportions in periodontally healthy and diseased subjects. This information will aid the army in identifying those individuals at risk for developing periodontitis and will contribute to better health care by providing new information concerning the molecular basis of increased susceptibility to and severity of periodontal disease.

**Progress:** This protocol was terminated by the principal investigator during FY07, due to several factors that made continuation of the study no longer feasible; i.e., loss of personnel from Fort Lewis and collaborators from the University of Washington (UW), and a change of priorities due to increased dental workload to support deployments and increased troop population. The nature of this study was such that there would have been no problem with an extended period of sample gathering; however, repeated attempts to contact the UW failed, which lead to the decision to terminate the project at MAMC with no further samples collected. Approximately 100 buccal cheek cell samples collected under this protocol were analyzed with PCR at the UW in 2004, and produced satisfactory DNA information.



## **Detail Summary Sheets**

Department of Emergency Medicine

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206063	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized Study of Capnography in Emergency Department Procedural Sedation		
<b>Principal Investigator:</b> CPT Nicholas N. Allan, MC		
<b>Department:</b> Emergency Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Brooks T Laselle, MC; MAJ Mark A. Denny, MC; CPT Joseph P. Mazzoncini, MC; LTC David A. Della-Giustina, MC		
<b>Start - Completion:</b> 7 Jun 2006 - Apr 2007	<b>Funding:</b> Oridion via The Geneva Foundation	<b>Periodic Review:</b> 7 Feb 2007

**Study Objective:** To determine if capnographic data recognizes respiratory depression during emergency department sedations that are not clinically recognized and whether these events are clinically important.

**Technical Approach:** This study is a prospective, blinded, randomized trial evaluating emergency physicians' use of capnography during consecutive procedural sedations on patients who sign informed consent to participate. Approximately 22 emergency physicians would be asked to consent for this trial. The physician may or may not have access to the capnographic data with each sedation. The physician will then complete the sedation as typical. The emergency physician should continuously evaluate the patient during the sedation as they normally would, however, if not blinded to the capnographic data, they may use this to assist in their decision making processes. The nurse observing the sedation will record the time to recovery and have the patient fill out the visual analog scales evaluating injection pain recall, procedural recall, and patient satisfaction. The physician completing the sedation will record, level of sedation, number of clinically recognized respiratory depression events, recognized complications, clinician interventions, and physician satisfaction. Study investigator will analyze the stored capnographic data looking for unrecognized complications and respiratory depression events. The groups will be compared by complication rates, incidence of interventions, incidence of respiratory depression events, level of sedation, time to recovery, injection pain, procedural recall, physician satisfaction, and patient satisfaction. A p-value of less than 0.05 will be considered statistically significant. Data will be analyzed using chi square, ANOVA, Kruskal-Wallis, and Mann-Whitney U-test methods.

**Progress:** Ten providers consented to participate; however no subjects (patients) have been enrolled due to a faulty recording device that was needed to initiate enrollment. A change of PI from Dr. Denny to Dr. Allan was submitted and approved during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207017	<b>Status:</b> Completed
<b>Title:</b> Retrospective Review of Emergency Department Deep Sedation Cases at One Military Medical Center		
<b>Principal Investigator:</b> MAJ Mark A. Denny, MC		
<b>Department:</b> Emergency Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC David A. Della-Giustina, MC; CPT Roger K. Manson, MC		
<b>Start - Completion:</b> 17 Nov 2006 - Apr 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to review and describe one year of experience with deep sedation cases completed by emergency medicine physician at Madigan Army Medical Center.

**Technical Approach:** This is a retrospective chart review to describe the experience of emergency physicians using deep sedation medications at one military medical facility. Approximately 80 to 100 deep sedation cases will be reviewed, all of which were completed over the last fifteen months. Data collected will be descriptive statistics including complications, interventions, indications for sedation, age, weight, time from last meal, type of medication, duration of procedure and time to discharge.

**Progress:** One-hundred cases were reviewed and Propofol/Etomidate was the preferred agents. There were relatively few complications (10%) with only two (2%) of these being major complications. All complications were brief and did not adversely affect patient outcome. This data is further support demonstrating the safety profile of deep sedation medications in the hands of experienced emergency physicians trained in sedation and advanced airway techniques.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207019	<b>Status:</b> Ongoing
<b>Title:</b> Impact of the ACGME Outcomes Project on Emergency Medicine Residencies		
<b>Principal Investigator:</b> Christopher S. Kang, MD		
<b>Department:</b> Emergency Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Christopher D. Yao, MC; MAJ Melissa L. Givens, MC		
<b>Start - Completion:</b> 20 Nov 2006 - Feb 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 5 Dec 2007

**Study Objective:** The objectives of this study are to provide an interim assessment of the impact, effectiveness and adoption rate of the ACGME Outcomes Project with respect to US Emergency Medicine Residency programs and provide a description of the utilization rates, ease of use, reliability and utility of the ACGME Outcomes Project Toolbox as obtained from Emergency Medicine Residency Program Directors.

**Technical Approach:** This a descriptive survey study of all US Emergency Medicine Program Directors (PD), Assistant Program Directors (APD), or Designated Institutional Officials (DIO) regarding the impact of the ACGME Outcomes Project on US Emergency Medicine Residencies (EMRs). This will also seek to elucidate the distribution of the various toolbox methods that are used in US Emergency Medicine Residency Programs potentially providing guidance in the selection of the most appropriate and applicable tools for the ACGME Outcomes Project in respect to EMRs. This study will also attempt to identify whether or not the various methods are being implemented properly. Descriptive statistics will be performed as necessary and applicable using the Chi-square test, Student t-test.

**Progress:** This minimal risk protocol was approved by the Expedited Review Committee 20 November 2006. A change in the role of PI was approved in June 2007, from CPT Yao to Dr. Kang. No continued data collection has been performed since May 2007 because of slow submission of completed surveys as well as CPT Yao's PCS. A new PI has been identified as well and the survey will be redistributed once a formal change of PI has been approved, around January - February 2008, now that initial permission and support of a national organization to distribute the survey has been obtained.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207024	<b>Status:</b> Ongoing
<b>Title:</b> A pilot study of maximum safe 2-3 hour serum acetaminophen levels in comparison to standard 4-hour levels in acetaminophen overdose		
<b>Principal Investigator:</b> CPT Tristan L. Knutson, MC		
<b>Department:</b> Emergency Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.; MAJ Melissa L. Givens, MC		
<b>Start - Completion:</b> 11 Dec 2006 - Dec 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 3 Dec 2006

**Study Objective:** The purpose of this study is to determine if a low (<100mcg/ml) 2-3 hour serum acetaminophen level correlates to a non-toxic 4 hour serum acetaminophen in patients who overdose on acetaminophen.

**Technical Approach:** Adult patients who present to the Emergency Department with acute overdoses of APAP will be offered enrollment. After consent, serum APAP will be drawn 2-3 hours post ingestion for data collection. The standard four hour level will also be drawn to guide all treatment decisions. Data including age, sex, substance ingested, time ingested, co-ingestants, drug and alcohol history, past medical history, presence of vomiting or decontamination will also be collected. No clinical decisions will be made with the 2-3 hour serum APAP level as it is being drawn for research purposes.

Statistics: 2-3 hour APAP levels will be collected and a cut off value of 100micrograms/mililiter (g/ml) will be used as a discriminatory level for non-toxic APAP ingestion. The 2-3 hour sample with a 100µg/ml cut point is expected to have a high sensitivity ( $\geq 0.99$ ) relative to the 4-hour determination at the 150µg/ml cutoff. The sample size is estimated to provide good precision for the 95% confidence interval for a sensitivity of 0.99. A sample size of 42 is need for precision of 0.03 and n=95 is needed for precision of 0.02.

Descriptive statistics and confidence will be used to describe the sensitivity and specificity of the earlier sampling time. We will determine the area under Receiver Operating Characteristic (ROC) by utilizing logistic regression models. McNemar's test can be used to assess differences if warranted. Other cut points for the 2-3 hours sample in addition to the 100µg/ml discriminatory level will also be assesses relative to the 4 hour sample and evaluated with the same methods.

**Progress:** This minimal risk protocol was approved by the Expedited Review Committee 11 December 2006. No progress has been made on this protocol. A change in the role of PI was approved from MAJ Givens to CPT Knutson; otherwise there have been no amendments to the study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207092	<b>Status:</b> Ongoing
<b>Title:</b> Effects of Intranasal Oxymetazoline on Pediatric Population 1-12 Months		
<b>Principal Investigator:</b> Neil B. Mullen, MD		
<b>Department:</b> Emergency Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Desislava Z. Hite, MD; CPT Nicole M. Giamanco, MC; CPT Jason M. Desadier, MC; CPT Jason R. Stone, MC; Andrew D. Dennis, LPN		
<b>Start - Completion:</b> 10 Jul 2007 - Jun 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objectives of this study of 1-12 month old subjects are to determine (1) effects of oxymetazoline intranasal application on heart rate, (2) effects of oxymetazoline intranasal application on blood pressure, (3) effects of oxymetazoline intranasal application on respiratory rate, (4) effects of oxymetazoline intranasal application on oxygen saturation, (5) if there is a change in respiratory pattern according to the modified pulmonary score scale provided by Smith et al, and to (6) examine subjective effects of oxymetazoline intranasal application (as described by parents).

**Technical Approach:** This is a preliminary safety study of using oxymetazoline in the pediatric population for the relief of nasal congestion, with the hypothesis that oxymetazoline administration will allow for increased patient comfort, decreased respiratory distress score, and improved physical exam by clinician, with minimal side effects. One month to 12 month old congested patients will be given oxymetazoline and evaluated for side effects on vital signs at pre administration, then 30 minutes and one hour post administration. Patients will be excluded if fever, vomiting, diarrhea, or chronic medical illnesses exist, since their treatment may significantly alter the vital signs and thus confound the results. Each patient will serve as his/her own control group since the triage vital signs are premedication (thus eliminating inter subject variability).

If patients qualify, parents will be informed of the study and consented. Triage vital signs will be recorded (blood pressure added after consent since it is not a usual vital sign in this age group) and oxymetazoline administered. Vital signs will then be recorded at time intervals 30 minutes and 60 minutes post administration. One hour is sufficient observation to note maximum effects, based on previous dose-response studies. At the end of the one hour, a free text section will be allowed for the parent to comment on the patient's behavior (irritability, drowsiness, general communication with parent), and a pulmonary score will be completed by physician (score modified from Smith et al, 1999). Immediately post study patients/parents will be offered free education on upper respiratory infection (URI) in the pediatric population and a hand out provided. The physician will be present and will answer any questions. The collected data will be stored under a code list and then summarized and analyzed. The results will be submitted for publication in ED journals and for presentation in ED/Peds conferences.

**Progress:** This greater than minimal risk protocol received initial IRB approval 22 May 2007, and final approval on 10 July 2007. An in-service on the protocol has been conducted. One infant has been enrolled and showed no change in vital signs of any clinical significance.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206059	<b>Status:</b> Completed
<b>Title:</b> Causes and consequences of patients who left a busy Army Medical Center Emergency Department prior to evaluation by a qualified health care provider		
<b>Principal Investigator:</b> CPT Adam S. Nielson, MC		
<b>Department:</b> Emergency Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Christopher S. Kang, MD		
<b>Start - Completion:</b> 31 Jan 2006 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The purpose of this study is to, first, describe the characteristics of the large number of patients who register for care at the MAMC-ED, then subsequently leave prior to evaluation by a qualified provider. Describing the characteristics of these patients should help identify where the MAMC health care system can make quality improvement changes to improve patient health care and access to a qualified provider. Secondly, the nature of the acuity of the illnesses or injuries that this population of patients represents will be described to determine if patients with severe illness are being permitted to leave prior to evaluation, subjecting the hospital and its providers to unnecessary liability. Patients will be contacted to determine the outcomes of their illnesses; i.e., did the patients seek care elsewhere, return to the MAMC-ED, hospitalized, or did the illness/injury improve on its own.

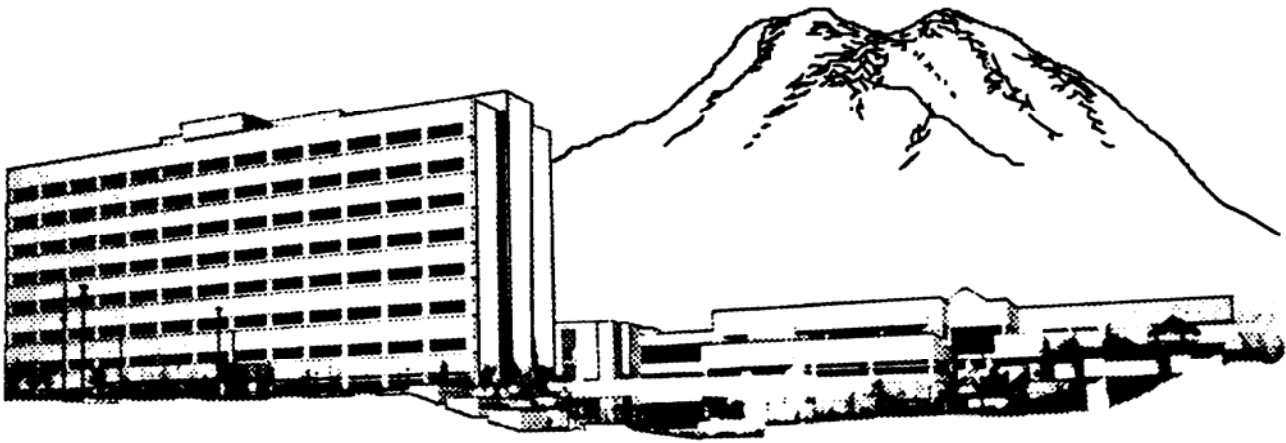
**Technical Approach:** Patients who leave the Madigan Army Medical Center-Department of Emergency Medicine, prior to being evaluated will be contacted by phone by the investigators and asked a standardized series of questions regarding the nature of their illness, what they have done to address it, why they left the emergency department prior to formal evaluation, and what could have been done to prevent their leaving.

**Progress:** Nearly 200 subjects participated prior to June 2006. Although less than the original goal, the current number of participants is larger than past studies (both referenced and reviewed). Data remains secured in Department of Emergency Medicine, although analysis has been delayed due to the deployment, and eventual PCS of the original PI, Dr. Nielson. The MAMC IRB decided to change the status of this protocol to "Completed," since no work was conducted on the study during FY07. Should Dr. Nielson return to MAMC, he may request reactivation of the protocol should data analysis show that more subjects are required to complete the project.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206078	<b>Status:</b> Ongoing
<b>Title:</b> Emergency Medicine/Combat Trauma Management Training Using Animal Models (Domestic Goat/ Capra hircus, Pig/Sus scrofa)		
<b>Principal Investigator:</b> MAJ Bradley N. Younggren, MC		
<b>Department:</b> Emergency Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Benjamin P. Harrison, MC; MAJ Brandon K. Wills, MC; Christopher S. Kang, MD; MAJ Robert B. Blankenship, MC; MAJ Melissa L. Givens, MC; MAJ Jacob A. Roberts, MC; MAJ Todd F. Baker, MC		
<b>Start - Completion:</b> 12 Apr 2006 - Mar 2009	<b>Funding:</b> DCI	<b>Periodic Review:</b> 11 Apr 2007
<b>Study Objective:</b> To effectively train providers combat-relevant resuscitative skills, focusing on preservation of life, limb, critical organ function, and casualty stabilization.		
<b>Technical Approach:</b> Training will utilize both inanimate (e.g. mannequin, cadaver, Sim Man, etc.) and live, anesthetized animal models. Whenever feasible, inanimate models will be used in place of live animals. Animal species used for this protocol will include goat and pig.		
<b>Progress:</b> This protocol provided training for 30 emergency medicine residents in three training labs.		



## **Detail Summary Sheets**

Department of Family Medicine

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205133	<b>Status:</b> Completed
<b>Title:</b> Prevalence of Hypertension in Active Duty Service Members		
<b>Principal Investigator:</b> COL Gary W. Clark, MC		
<b>Department:</b> Family Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LCDR Brian A. Smoley, MC, USN		
<b>Start - Completion:</b> 7 Sep 2005 - Dec 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 14 Aug 2006

**Study Objective:** To use screening blood pressure measurements collected during mandatory wellness screenings to estimate the prevalence of hypertension in a population of active duty service members at Fort Lewis.

**Technical Approach:** This will be a retrospective, cross-sectional analysis of data collected on approximately 10,000 active duty service members who presented for wellness screenings through the I Corps Readiness and Outcomes Wellness Service (ICROWS) between January 1 and December 31, 2004. Data on measured blood pressure and self-reported age, rank, gender, race/ethnicity, and use of blood pressure medications will be collected from the ICROWS database without any inclusion of or reference to individual identifying information. Measured blood pressure and self-reported use of blood pressure medications will be used to estimate the prevalence of hypertension in the study population. Age-specific and age-adjusted prevalence of hypertension will be reported using descriptive statistics. Relationships between hypertension and demographic variables will be explored through bivariate and/or multivariate analyses.

**Progress:** This protocol was reported as completed during FY07. Results: Of 15,735 service members with health risk assessments recorded for 2004, 15,391 (98%) met all of the study's inclusion criteria. Those excluded included 323 who were missing a blood pressure measurement, 19 who were missing a demographic variable, and 2 who were outside of the study's age range.

The mean age in the study population was 28 years, mean blood pressure was 127/69 mmHg, and mean body mass index was 25.5 kg/m<sup>2</sup>. Approximately 2% of subjects reported using medicine for high blood pressure. The overwhelming majority were less than 40 years old (90%) and male. Approximately 17% (417) of the subjects categorized as "Hispanic" more specifically self-reported themselves as Black Hispanic. The race/ethnicity group "Other" included 290 American Indians or Alaska Natives (13%), 704 Asians/Orientals (31%), and 378 Pacific Islanders (17%).

The prevalence of hypertension was 13% overall and 11% in those less than 40 years of age. Hypertension was more common in older age groups, men, Blacks, and those in the senior ranks. The age-adjusted prevalence of hypertension was 21% for men and 15% for women. Hypertension was treated in 285 (15%) of all cases, 124 (8%) of cases in subjects less than 40 years of age, and 161 (37%) of cases in subjects 40-65 years of age, yielding treated hypertension prevalences of 2% overall, 1% in those less than 40 years of age, and 10% in those 40-65 years of age. After controlling for all 5 subject characteristics, age, body mass index, Black race/ethnicity, and senior rank were all associated with increased odds of having hypertension. Rank and age were noted to be moderately correlated (Spearman's rank coefficient = 0.65).

Hypertension was further explored through a stratified examination of blood pressure categories in the 15,106 subjects who did not report taking medicine for high blood pressure. Pre-hypertension was the most prevalent category (63%) followed by normal blood pressure (26%) and then stage 1 and stage 2 hypertension (10% and 1%, respectively). Multivariate logistic regression showed pre-hypertension to be independently associated with body mass index, male sex, and senior rank (p values < 0.01, < 0.01, and 0.01, respectively) but not age or race/ethnicity. The age-

adjusted prevalence of pre-hypertension was 65% for men and 50% for women.

A sensitivity analysis that decreased the observed blood pressure readings in those with pre- and stage 1 hypertensive readings by 7/4 mmHg estimated the prevalence of hypertension and pre-hypertension after the removal of the white coat effect to be 6% and 49%, respectively.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207118	<b>Status:</b> Ongoing
<b>Title:</b> Cervical Abnormalities in Routine Papanicolaou Smears in Women Over Age 65		
<b>Principal Investigator:</b> CPT Jason C. Clark, MC		
<b>Department:</b> Family Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Gary W. Clark, MC; Erin L Guex-Clark, M2, MS		
<b>Start - Completion:</b> 24 Aug 2007 - 10/07	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this protocol is to describe efficacy of cervical cancer screening in women greater than 65 years of age.

**Technical Approach:** This study will be a descriptive analysis of all pap smears done between 2001 and 2006, for women older than 65. A positive screening test will include all diagnoses that require follow-up testing per the ASCCP guidelines, primarily colposcopy or diagnostic excision procedures. A true positive result will be tissue confirmed diagnosis of CIN I and above, as these diagnoses carry a high enough risk of progression to warrant excision per the ASCCP guidelines. Investigators can then calculate a positive predictive value for women at Madigan over the age of 65 for the liquid (or "thin layer") Papanicolaou smear. Investigators will also look at all of the cervical cancer diagnoses in this period, and look retrospectively at the screening history of those individuals.

**Progress:** This minimal risk protocol received final approval by the Expedited Review Committee, effective 24 August 2007.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205124	<b>Status:</b> Completed
<b>Title:</b> Racial Differences in Health Outcomes for Adults with Diabetes in a Military Setting		
<b>Principal Investigator:</b> LTC Telita D. Crosland, MC		
<b>Department:</b> Family Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 23 Aug 2005 - Jul 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 10 Aug 2006

**Study Objective:** To evaluate health outcomes for diabetic patients based on race in a military setting.

**Technical Approach:** This study is a quantitative cross-sectional analysis of approximately 5,000 adult patients in the MAMC diabetic database. Data to be recorded includes: race, age, rank, low density lipoproteins, hemoglobin A1C, blood pressure, micro albumin, and number of clinic visits. Descriptive statistical analysis will be used to determine if there is a statistical and clinical difference in health outcomes in the diabetic patient based on age.

**Progress:** Completed the data collection and analysis. Working on the abstract. No further enrollment or data request is anticipated.

**Results:** There were 3789 patients who met the inclusion criteria; 48% Caucasians, 8 % African-American, 5.6% Asian, 5.1 % others and 11.1% unknown. Mean SBP was 137.3 mmHg, DSBP was 71.4 mmHg, HbA1C was 7.06 % and LDL was 92.6 mg/dl. After controlling for gender, age and rank, race was associated with a significant difference in SBP, DSBP, LDL and A1C. There was no significant difference in receiving urine test for protein.

**Conclusions:** Minorities are more likely to have a higher blood pressure, LDL and HbA1C in a health care system that provides universal health coverage. This study suggests that access alone does not completely account for health care disparities.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204117	<b>Status:</b> Completed
<b>Title:</b> Impact of the Sole Prescriber Program on Use of Opioid Medications and Quality of Life		
<b>Principal Investigator:</b> COL Diane M. Flynn, MC		
<b>Department:</b> Family Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Guy P. Runkle, MC; Steven J. Konicek, MD; Nancy A. Poffenberger, PAC, Ph; Claudia N. Swenson, PhD; Gary J. Revello, RPh; Helen E. Holt, ARNP; LTC Mary T. Bennett, AN; LTC Elizabeth C. Shanley, MC		
<b>Start - Completion:</b> 31 Aug 2004 - Dec 2004	<b>Funding:</b> DCI	<b>Periodic Review:</b> 14 Aug 2006

**Study Objective:** This protocol is designed to determine if enrollment of Madigan patients identified as being high utilizers of narcotic medication into a sole prescriber program results in a decrease in escalation of narcotic use and an improvement in patient satisfaction. Secondary objectives include determination of the impact of the sole prescriber program on continuity of care, utilization of services and quality of life.

**Technical Approach:** An estimated 50 MAMC patients who have received more than 7 prescriptions from the MAMC pharmacy for opioid medications per quarter during all of the first three quarters of FY2004 will be randomized into two groups: (1) immediate and (2) delayed enrollment in the Sole Prescriber Program. Patients randomized for immediate enrollment will be enrolled starting 1 October 2004. Delayed enrollment will begin 1 February 2005. The groups will be compared with regard to monthly dosage of opioid medications expressed in morphine equivalent dosage, number of prescribers of narcotics per patient, and several measures of utilization of clinical services. In addition, patient satisfaction and quality of life will be measured at baseline and after three months in both groups.

The following dependent variables will be compared between study groups using the paired t-test: (1) Change in morphine equivalent dosage of narcotics, (2) Mean number of prescriptions for narcotics per patient per quarter, (3) Mean number of prescribers of narcotics per patient per quarter, (4) Mean number of ER visits per patient per quarter, (5) Mean total MAMC visits per patient per quarter, (6) Mean total visits to health care facilities in community billed to TRICARE per patient per quarter, and (7) Score on quality of life survey. The following binary dependent variables will be compared between study groups using the McNemar's test: (1) At least one visit to primary care provider per quarter (Yes/No), and (2) Is a narcotic agreement recorded in the electronic medical record (Yes/No). The 5-item patient satisfaction survey will be analyzed using the Wilcoxin-Signed rank test.

**Progress:** This protocol was reported as completed in January 2007. Only eight of the 38 estimated subject population consented to be in the study. Four of these were in the intervention group, four in the control group. No significant differences were found, mostly due to the small sample size, although telephone surveys alone seem to improve satisfaction.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206105	<b>Status:</b> Ongoing
<b>Title:</b> Implementation of an Office-Based Screening Tool to Improve Adherence with Recommended Preventive Services in Primary Care		
<b>Principal Investigator:</b> COL Diane M. Flynn, MC		
<b>Department:</b> Family Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Gary W. Clark, MC; LTC Ross E. Colt, MC; LTC Kathryn K. Ellis, MC; CPT Andrea S. Otto, MC; Janet O. Schertzer; John G. Meyer, MD, MPH		
<b>Start - Completion:</b> 5 Jul 2006 - Dec 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 4 Oct 2007

**Study Objective:** To determine if the use of a questionnaire and written instructions at every primary care visit to assess adherence with recommended preventive services will increase rates of recommended preventive services.

**Technical Approach:** Beginning 1 July 2006, all patients presenting for care at Madigan Family Medicine Clinics will be asked to complete a preventive services checklist to determine if they are up to date on recommended preventive services. The nurse or nursing assistant who screens the patient will assist the patient in completing the questionnaire as needed, will distribute appropriate educational materials as indicated and will order indicated labs and studies under the primary care provider's name. The provider who sees the patient will perform any indicated examination and order any indicated labs or studies as time permits. If time does not permit addressing preventive services, the patient will be instructed to make a follow up appointment for a periodic physical examination. Rates of adherence with recommended preventive services will be compared between the pre-intervention and post-intervention periods between patients seen in the Gold Team and those seen in other Family Medicine Clinic teams. Data will be prepared by the Health Outcomes section and will be devoid of patient identifiers.

**Progress:** Beginning 11 September 2007, all 6,608 patients who presented for care in the Family Medicine Clinic Gold Team (intervention group) were asked to complete a survey to determine if they were up to date on recommended preventive studies. The intervention period continued for 4 months. Investigators are now comparing adherence with preventive studies between the gold team with the other FMC teams (control group). Analysis has been completed for mammograms; but the study remains ongoing to complete analysis for other preventive interventions.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207001	<b>Status:</b> Ongoing
<b>Title:</b> Cardiovascular Risk Factor Identification in Active Duty Soldiers Over the Age of 40 Years		
<b>Principal Investigator:</b> COL Diane M. Flynn, MC		
<b>Department:</b> Family Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Cathy J. Bailey; John G. Meyer, MD, MPH; Nancy A. Cox, RN, BSN; COL (Ret) Charles A. Andersen, MD; CPT Jason T. Perry, MC; MAJ Jeremy D Johnson, MC		
<b>Start - Completion:</b> 6 Oct 2006 - Apr 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 4 Oct 2007

**Study Objective:** The objectives of this study are to (1) screen active duty service members over the age of 40 for cardiovascular risk factors in order to identify opportunities for risk reduction, and (2) determine the degree to which active duty soldiers identified to have cardiovascular risk factors follow advice to follow up with primary care for further evaluation and management.

**Technical Approach:** All 163 service members age 40 or older assigned to I Corps HQ will be invited to participate. They will be instructed to have fasting lipids and glucose labs drawn at least one week prior to the outreach event. To facilitate lab draws, an on-site phlebotomy team will draw fasting labs in the HQ vicinity on 10 October 2006. Participants who go to the on-site lab draw will be consented to participate in the study prior to phlebotomy. Participants will also be permitted to go to the lab at MAMC, Okubo or Nisqually if they prefer. Each participant will be scheduled for an appointment on 19 October between 0800 and 1600. Tobacco users will be asked to refrain from using tobacco for the two hour period prior to their appointment. Upon arrival, those who did not participate in the 10 October on-site lab draw, will be asked for consent to participate in the study. Tobacco users will be asked the time they last used tobacco. Participants will complete a cardiac risk survey and will have the following measurements and assessments performed: BP, waist circumference, cardiac rhythm strip, carotid duplex scan, and FMD. Regarding FMD, the following protocol will be followed. Patients will be allowed to rest supine in a climate-controlled room for 10 minutes preceding the examination. A blood pressure cuff will then be placed as far proximal on the left arm as is practical. A single measurement of the brachial artery diameter and blood flow velocity and waveform will then be made immediately adjacent to cuff (to standardize repeat measurements). The blood pressure cuff will be inflated to 50 mm Hg greater than systolic blood pressure for 5 minutes. The cuff will then be deflated and the brachial artery diameter and blood flow velocity measured again at 1 and 2 minutes after cuff deflation. FMD will then be calculated as the change in diameter divided by the resting diameter. Participants will also be queried to determine if they are up to date on screening tests for cervical, breast, prostate and colorectal cancer. After all studies are completed, a nurse or provider will sit down with each participant and review their cardiac risk profile and cancer screening background. Any individual who has unmanaged cardiac risk factors or is not current with cancer screening tests will be advised to follow up with their primary care clinic.

**Progress:** This minimal risk protocol received approval by the Expedited Review Committee 6 October 2006. All 76 subjects underwent the original risk factor assessment in October 2006. Those who were identified as having unmanaged cardiac risk factors were instructed to follow up with primary care. Six months later, subjects' medical records were examined to determine if they had followed up as instructed. In July 2007 subjects who had not yet followed up were surveyed to determine why they did not follow up. Investigators continue to accept survey responses at the time of this report.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207116	<b>Status:</b> Ongoing
<b>Title:</b> Urine Culture in the Primary Care Management of Urinary Tract Infections in Adult Females: Does it Decrease Follow-up Visits?		
<b>Principal Investigator:</b> MAJ Jeremy D Johnson, MC		
<b>Department:</b> Family Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Hyrum F. Durtschi, MC		
<b>Start - Completion:</b> 14 Aug 2007 – Jul 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 13 Aug 2007

**Study Objective:** Primary aim of this study is to determine if there is a difference in the percentage of follow-up visits for continued UTI symptoms in a two week period after initial diagnosis of urinary tract infection in a cohort who had a urine culture completed as part of their primary management compared a cohort without a urine culture completed.

Secondary aims of this study are to determine (1) if there is a difference in the percentage of patients changed to a different antibiotic in the two weeks after initial treatment for UTI in the group with urine culture and the group without urine culture, (2) the percent of nonpregnant and non-diabetic women, age 18-65, diagnosed with urinary tract infections that have a urine culture ordered as part of their management, (3) which medicines, and for what duration, providers use for the management of urinary tract infections and at what percentage, (4) what percent of urine cultures ordered from the subset in question 2 grow a specific bacteria as defined by greater than or equal to 1,000 colony forming units per ml which is the Infectious Diseases Society of America consensus definition of cystitis in antimicrobial treatment studies, (5) what percent of urine cultures ordered grow a bacteria that is resistant to the antibiotic initially prescribed by the health care provider, and (6) what percent of those patients whose urine grew bacteria that is resistant to the antibiotic initially prescribed by the health care provider were changed to a new antibiotic.

**Technical Approach:** This research protocol is a retrospective chart review, looking at 1,067 nonpregnant and non-diabetic women assigned to Madigan Family Medicine or Internal Medicine that are 18-65 years old and diagnosed with an uncomplicated UTI (urinary tract infection). The diagnosis of UTI will be obtained from the ambulatory data module and subjects will then be assessed for inclusion and exclusion criteria. Information will be collected on age, race, smoking status, provider status (i.e. physician, PA, NP), urinalysis results, urine culture results, medications used in treatment, and follow-up visits made. The main outcome variables are whether a follow-up appointment is made and whether a second antibiotic is prescribed. These outcome variables will be compared to whether a urine culture was obtained (yes or no) using the Chi square test. Other outcome variables will be described using means, standard deviations, and percents.

**Progress:** This minimal risk protocol received final approval by the Expedited Review Committee, effective 14 August 2007.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205130	<b>Status:</b> Ongoing
<b>Title:</b> Use of Pedometers Among Healthcare Providers in a Large Military Family Medicine Department		
<b>Principal Investigator:</b> CPT Kevin M. Kelly, MC		
<b>Department:</b> Family Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Alvin Y. Tiu, MC; MAJ Robert C. Oh, MC; CPT Jarret E. Sands, MC; LTC Telita D. Crosland, MC		
<b>Start - Completion:</b> 30 Aug 2005 - Aug 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 29 Aug 2006

**Study Objective:** To determine the affect of a pedometer exercise program on the level of physical activity of health care providers in a primary care clinic.

**Technical Approach:** This study sets out to determine the affect of a pedometer exercise program on the level of physical activity of health care providers in a primary care clinic. Residents, faculty, and mid-level providers in the MAMC Family Medicine Department, approximately seventy total subjects, will be enrolled in the study. Study subjects will be evaluated for baseline physical activity level category with the International Physical Activity Questionnaire (IPAQ) and baseline daily step count. They will be given a pedometer and instructions on increasing their daily activity level. Their daily step count will be followed for six weeks. The IPAQ will be repeated post intervention. A pre and post intervention BMI and blood pressure will be also measured. The change in number of steps taken per day, METS/day, and physical activity category (sedentary, low active, somewhat active, active, highly active) will be statistically analyzed correlated to independent variables of age, BMI, and blood pressure. Differences between staff, residents, and mid-level providers will also be evaluated.

**Progress:** This protocol closed to enrollment with 50 providers (subjects) enrolled. The subjects completed their six week pedometer course and returned their surveys and log books to the principal investigator. The information has been entered into a database; study staff is in the process of analyzing the data and writing up the project. Anticipate completion of data analysis in FY 2008.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206048	<b>Status:</b> Completed
<b>Title:</b> A Randomized, Controlled Trial of Manual/Manipulative Therapy for Acute Low Back Pain in Active Duty Military Personnel: A Pilot Study		
<b>Principal Investigator:</b> MAJ Douglas M. Maurer, MC		
<b>Department:</b> Family Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Scott T. Stoll, D.O., Ph.D.; CPT Hillary Arnold, DO; CPT Jarret E. Sands, MC; CPT April E. Lynch, MC; Tonya N. Kozminski, MD; MAJ David L. Brown, MC; CPT Hyrum F. Durtschi, MC; COL Gary W. Clark, MC; CPT Scott P Grogan, MC; CPT Richard J. Geshel, MC; LTC Charles W. Webb, MC		
<b>Start - Completion:</b> 21 Mar 2006 - Feb 2007	<b>Funding:</b> Samueli Institute for Information Biology	<b>Periodic Review:</b> 23 Jan 2007
<p><b>Study Objective:</b> To evaluate the efficacy of conservative, non-surgical, manually applied biomechanical treatments to reduce pain and improve function in young adult active duty military personnel with acute low back pain.</p> <p><b>Technical Approach:</b> This is a prospective, randomized, blinded, controlled clinical trial that plans to enrollment male and female Soldiers ages 18-25 consecutively from all military personnel presenting during sick call to the Acute Care Clinic, Department of Family Medicine, Madigan Army Medical Center, Fort Lewis, Washington. Informed consent will be obtained from the subjects who desire to participate in the study by the Clinical Research Coordinator (CRC) and assigned randomly to treatment (M/MT) or control (Standard Care) groups. The Study Evaluating Physician (SEP) will perform a routine exam to address the exclusion criteria. If the patient is not cleared for the study by the SEP s/he will enter routine care and be excluded from the study. If the subject is cleared for the study by the SEP, the subject will be given an appointment with a Study Treatment Provider (STP). The subject will be informed of the study group assignment and treatment initiated. All subjects will be scheduled to see the same STP for all study treatment visits. All subjects from both treatment and control groups will see the SEP for evaluation regarding modified duty assignment. The SEP and CRC will be blinded to group assignment. For this study, standard care will include prescribed medications including acetaminophen, ibuprofen or naprosyn, cyclobenzaprine for up to one week; acetaminophen with codeine for up to 1 week; passive modalities (ice, heat) for symptomatic relief; handouts on back self-care and exercises. Subjects will be reevaluated at 2 weeks and 4 weeks for improvement. The treatment group will receive manual/manipulative therapy (M/MT) in combination with standard care. M/MT involves a set of treatments with elements of both osteopathic manipulative and chiropractic techniques and sessions will be given up to twice a week for up to four weeks.</p> <p>Pain will be measured using the Visual Analog Scale and quantification of medication use. Functionality will be assessed using the Roland Morris Questionnaire, Back Pain Functional Scale, and days on limited duty. Statistical analysis tools will include: descriptive statistics, cross tabulations and measures of association, chi-square for dichotomous variables, and a 2x3 mixed factorial ANOVA. Three one-way ANOVAs comparing the treatment groups on pain, functionality, medication use and other outcome scores will be performed using residualized improvement scores.</p> <p><b>Progress:</b> This protocol was reported as completed in June, 2207, with 63 subjects enrolled, 33 in OMT (treatment) group and 30 in standard care (control) group. The OMT group showed significant improvement in pain on the VAS questions for "pain now" (<math>p &lt; 0.05</math>) and "typical pain" (<math>p &lt; 0.05</math>) at follow-up. The OMT group showed significant improvement in function on RMQ (<math>p &lt; 0.05</math>) and the BPFS (<math>p &lt; 0.05</math>) at follow-up. Although the mean days of limited duty was lower in the OMT group compared to the standard care group (18.9 vs 19.3), the difference was not statistically significant. The OMT group reported significantly greater patient satisfaction (<math>p &lt; 0.05</math>)</p>		

and overall improvement ( $p < 0.05$ ) when compared to the standard care group. In this pilot study of young active duty military soldiers, a standardized protocol of OMT added to standard care was significantly more effective than standard care alone at reducing pain, improving function, increasing patient satisfaction and overall improvement. Treatment effect sizes were moderate to large for all significant findings and the study proved to be safe and feasible in the military family medicine settings. Further studies should be performed on larger populations utilizing a sham protocol to further investigate the effect of OMT on acute low back pain.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207006	<b>Status:</b> Ongoing
<b>Title:</b> Analysis of End-of-Life Care in Elderly Military Beneficiaries: A Pilot Study		
<b>Principal Investigator:</b> Thomas C. Michels, MD		
<b>Department:</b> Family Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 20 Oct 2006 - Sep 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 25 Sep 2007

**Study Objective:** The aim of this descriptive pilot study is to characterize the end-of-life (EOL) experience of elderly military beneficiaries by examining their inpatient and outpatient medical records over the last three years of life. Specifically: Aim 1: Analyze the demographic characteristics, disease burden, and healthcare utilization of elderly (age >65) military care eligible beneficiaries who die within military treatment facilities (MTFs) via systematic review of medical records from the last three years of life, and Aim 2: Evaluate the quality of this care at military treatment facilities (MTF) using the end-of-life care standards from the Assessing Care of Vulnerable Elders (ACOVE) project and the Beers Criteria for Potentially Inappropriate Medication (PIM) use. Aim 3: Based on Aims 1 and 2, site specific and possibly system-wide recommendations will be made to enhance EOL care within MTFs.

**Technical Approach:** A random sample of inpatient and outpatient records of elderly patients who died at selected MTFs will be reviewed using standardized chart audit tools to assess the above conditions and relevant patient demographic data. Records from approximately 110 decedents will be reviewed in the entire study, with approximately 15 reviews coming from MAMC. Data analysis will examine the frequency of specific findings found from the chart reviews. Continuous variables will be summarized as means with 95% confidence intervals (CIs). The results of this study will be used to improve quality of care within MTFs to future patients by using performance improvement processes. This characterization of EOL experiences will enhance military health care planning as care demands increase for this population.

**Progress:** This minimal risk protocol received approval by the Expedited Review Committee 20 October 2006. Based on a 10% sample, eight charts are being reviewed, all inpatient and outpatient records in the three years prior to death. There was initially some difficulty finding patients for which all inpatient and outpatient records were available, but this was relatively minor. Four patients had records reviewed, data abstracted onto the data collection forms included in the IRB protocol, and the anonymous forms mailed to the study coordinator at USUHS. Three more patients' records are now completed, and the fourth, and final, patient's records are in the process of review. Once data collection is complete, these will be mailed to the coordinator as well, thus completing Madigan's contribution to this study. Patients from all the sites involved will be analyzed in aggregate by the USUHS coordinator.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206104	<b>Status:</b> Ongoing
<b>Title:</b> Implementing a Medical Ethics Curriculum in a Family Medicine Residency: Assessment of Need, Description of the Process, and Evaluation of Effectiveness		
<b>Principal Investigator:</b> LCDR Richard W. Sams, MC, USN		
<b>Department:</b> Family Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Susan P. Opar, MC		
<b>Start - Completion:</b> 5 Jul 2006 - Jun 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 6 Jun 2007

**Study Objective:** The objectives are: (1) to assess family medicine residents and staff's baseline level of knowledge and comfort level in dealing with ethical issues in medicine, (2) to implement a medical ethics curriculum in the family medicine residency, describe the curriculum's content and implementation process and (3) to evaluate any gains in knowledge and comfort level from the educational intervention and participants' perceived value of the curriculum.

**Technical Approach:** All faculty and residents will be invited by email (Attachment #1) and announcements to participate in the study. They will be made aware that comparisons will be made of their LNA and post-test curricular survey. The numbered LNA tool will be placed in their mail boxes. They will be asked to return the completed tools to the associate investigator's mailbox. The curriculum will be implemented by integrating each 45 minute seminar into the already existing CME schedule. Four forty-five minute didactic sessions occur each Wednesday morning for CME and GME. Once per rotation block, a medical ethics seminar will be conducted by the PI during one of the four didactic sessions. The syllabus developed by the PI will serve as the template for the sessions. All members of the faculty and residents are encouraged to attend the CME lectures in general. At the one year mark the post-test curricular survey tool will be placed in all faculty and residents mailboxes, and they will be asked to complete the survey at that time. The post-test curricular surveys will have the same number for each person who completed the LNA. This information will then be analyzed. See the attached curriculum, which contains the syllabus, LNA and post-test / curricular survey.

The knowledge portion of the LNA and post-test consist of 10 multiple choice case-based questions, with one correct answer for each question. Each case has a corresponding question regarding how comfortable the person is with the described ethical dilemma and how to resolve it. The person is to respond by rating his or her level of comfort on a 10 point Likert scale. The LNA and post-test / curricular survey assesses the person's perceived value of the ethics training for preparing him or her to address similar ethical issues. This is assessed on a 10 point Likert scale. The LNA tool assesses how burdensome the LNA was to complete on a 10 point Likert scale. The post-test / curricular survey also assesses the following: participants perceived value of the curriculum personally and professionally; how many seminars were attended; and an assessment of was there too little, too much or the right amount of emphasis on medical ethics.

**Progress:** During FY07, a total of 41 participants (family medicine residents and staff) received the pre-test, with a 68% response rate. The ethics curriculum was implemented with monthly sessions over the academic year 2006-2007. The post-test will be distributed to the same residents and staff shortly, at which time a final data analysis will be performed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206080	<b>Status:</b> Ongoing
<b>Title:</b> Predicting Intern Performance using an Objective Structured Clinical Examination		
<b>Principal Investigator:</b> MAJ Matthew W. Short, MC		
<b>Department:</b> Family Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Robert B. Blankenship, MC; MAJ Jennifer E. Jorgensen, MC; COL Bernard J. Roth, MC		
<b>Start - Completion:</b> 18 Apr 2006 - Aug 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 3 Apr 2007

**Study Objective:** To determine if intern performance on an Objective Structured Clinical Examination (OSCE) prior to internship is more predictive than prior academic performance in identifying potential deficiencies in Accreditation Council for Graduate Medical Education (ACGME) core competencies during the intern year.

**Technical Approach:** Sixty-one incoming clinical interns at Madigan Army Medical Center will complete an Objective Structured Clinical Examination (OSCE) during their intern orientation. This OSCE will evaluate each intern based on the Accreditation Council for Graduate Medical Education (ACGME) core competencies of patient care, medical knowledge, practice-based learning and improvement, interpersonal and communication skills, professionalism, and system-based practice. The objective of this study is to determine if intern performance on an OSCE prior to internship is more predictive than prior academic performance based on data from their First Year Graduate Medical Education (FYGME) application in identifying potential deficiencies in ACGME core competencies during the intern year. If the OSCE is more predictive of internship performance, deficiencies in ACGME core competencies identified during this examination could be remedied earlier to ensure successful completion of internship and result in more competent, caring physicians.

**Progress:** This is an educational research project using a clinical examination done on incoming interns and evaluation of their performance throughout the year. Since initial data collection, Program directors have completed questionnaires on their interns' performance. There will be a repeat clinical examination in June 2007 of the same intern class. The protocol remains ongoing to complete analysis.



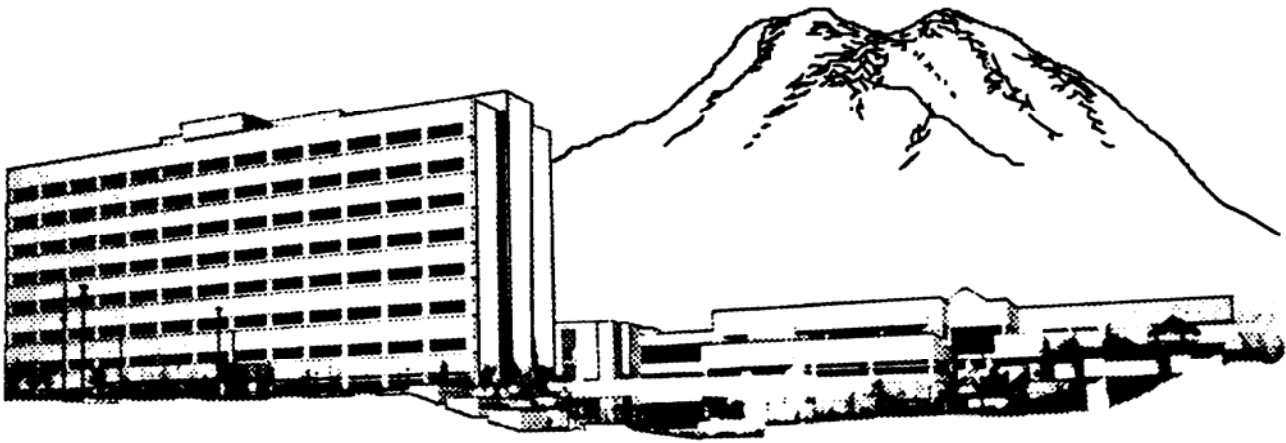
### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207012	<b>Status:</b> Ongoing
<b>Title:</b> Colonoscopy by a Family Physician: A Case Series Comparing a Family Physician to a Gastroenterologist to Competency Standards		
<b>Principal Investigator:</b> MAJ Matthew W. Short, MC		
<b>Department:</b> Family Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Khalid A. Jaboori, MC; CPT Leigh D. Johnson, MC; CPT Jason E. Domagalski, MC		
<b>Start - Completion:</b> 27 Oct 2006 - Oct 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 26 Nov 2007

**Study Objective:** To show that a family physician can perform diagnostic colonoscopy as safely and accurately as board certified gastroenterologists.

**Technical Approach:** Colonoscopy procedure reports will be reviewed from 1818 patients and data compiled using a spreadsheet to record the items listed. An electronic record review will be performed for at least six months following the procedure date to document any complications, missed diagnoses, or needs for additional referrals or studies. Pre-procedure: appropriate indication; informed consent; use of recommended post-polypectomy and post-cancer resection surveillance intervals; use of recommended ulcerative colitis and Crohn's colitis surveillance; colon preparation documented. Intra-procedure: cecal intubation rates; detection of adenomas; withdrawal times; biopsy specimens obtained in patients with chronic diarrhea; number and distribution of biopsy samples in ulcerative colitis and Crohn's colitis surveillance; mucosally based pedunculated polyps and sessile polyps <2 cm in size sent for surgical resection without an attempt at endoscopic resection or documentation of endoscopic inaccessibility. Post-procedure: incidence of perforation; incidence of post-polypectomy bleeding; post-polypectomy bleeding managed non-operatively. Other: patient age, patient Gender, location of biopsies, location of polypectomies, pathology results, final diagnosis, time to cecum, total procedure time, medication type and dosage, missed diagnoses, need for additional referrals or studies, and concurrent EGD findings in those patients receiving a colonoscopy for iron deficiency anemia.

**Progress:** This minimal risk protocol received initial approval by the Expedited Review Committee on 27 October 2006. An amended protocol was submitted 23 September 2007, requesting review of 218 additional family medicine procedure charts to further strengthen the study with additional scopes that have been performed since the time of the original protocol approval. The title has been changed from "Colonoscopy by a Family Physician: A Case Series of 1600 Procedures Comparing a Family Physician to a Gastroenterologist" to "Colonoscopy by a Family Physician: A Case Series Comparing a Family Physician to Gastroenterologists to Competency Standards."



## **Detail Summary Sheets**

Health Outcomes Management Division

## Detail Summary Sheet

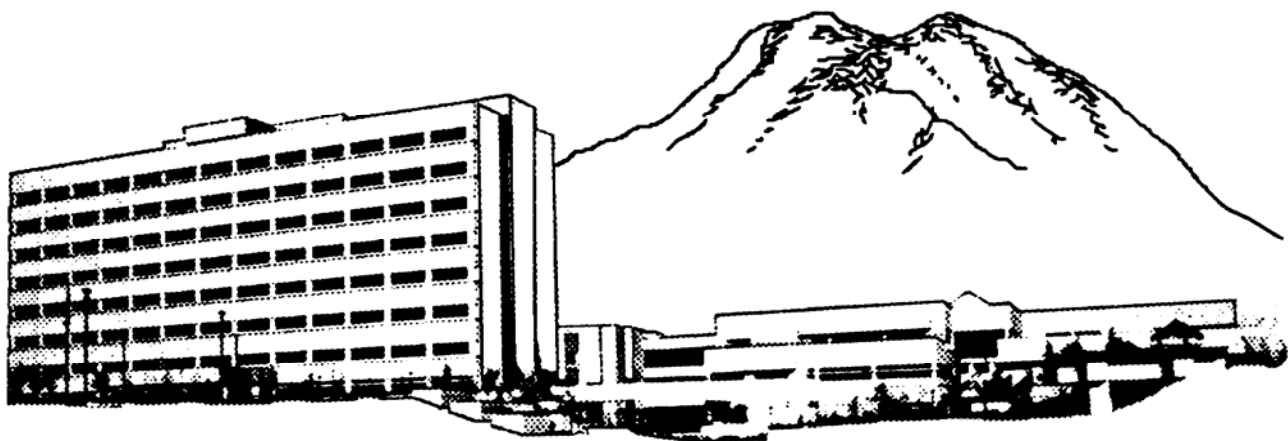
<b>Date:</b> 30 Sep 07	<b>Number:</b> 205108	<b>Status:</b> Terminated
<b>Title:</b> The Deployment of Physical Therapy for Combat: A Description of the Process and Outcomes		
<b>Principal Investigator:</b> John G. Meyer, MD, MPH		
<b>Department:</b> Outcomes	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Mona O. Bingham, AN; MAJ Daniel M. Jayne, MC; CPT Brian W. Jovag, MC		
<b>Start - Completion:</b> 21 Jul 2005 - May 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 29 Jun 2006

**Study Objective:** The overall goal of this study is to describe injuries and the impact of providing physical therapy evaluation and treatment intervention prior to and during combat deployment for a brigade (BDE) of soldiers. There are 5 specific aims to meet this overall goal. Using data already collected from computerized medical records and hospital information systems, the aims of this secondary data analysis study are: (1) Describe a BDE of soldiers anticipating immediate deployment and specifically those with physical orthopedic complaints and injuries. (2) Describe the impact of pre-deploying screening and intervention for orthopedic complaints in a deploying BDE. (3) Compare orthopedic health and injuries of soldiers in an AD BDE versus soldiers in an Army National Guard (ARNG) BDE. (4) Describe the impact of physical therapy care provided in the field environment for a combat BDE during a combat deployment. (5) Compare pre-deployment Health Risk Assessment II (HRA II) results to post-deployment HRA II results.

**Technical Approach:** For this retrospective study, data will be obtained from the computerized medical records available at Madigan Army Medical Center (MAMC) and other health information system collected as part of the SRP. The population of soldiers assigned to the 81st BDE and the 3rd BDE (and additional units who provided support or were supported by the BDEs during this deployment) who completed the Soldier Readiness Process (SRP) prior to deployment, immediately post deployment, and 90-days post deployment will be examined to meet the study goals. This number is anticipated to be no more than 75% of the BDEs. However descriptive data from the SRP process on the Health Risk Appraisal II (HRA II) of both BDEs will be collected to adequately describe the differences and similarities between the 2 BDEs. Data will be collected on a number of outcome variables including: demographic data, and number of soldiers in BDE who self-reported pain, made PT self-referrals, SRP PT referrals, returned via Medical evacuation, seen for healthcare in theater by PT and other PCP. Other outcome variables include: lost work time, medical convoy hours, number of PT treatment procedures, number of injuries, type of injury/diagnosis, time soldier not able to perform combat mission, number of follow-up physical therapy visits, profile type and length, pain level as determined by physical therapist, final disposition, and HRA II limited activity answers.

The analysis plan includes a number of different analysis techniques to answer the research questions/objectives. SPSS will be used to run all descriptive statistics (means, standard deviations, percentages). To compare orthopedic health and injuries of soldiers in an AD BDE versus soldiers in an Army National Guard BDE], Chi-square will be used for categorical variables and either T-tests or Mann-Whitney U tests for measured variables to determine relationships. ANOVA will be used to determine relationships for interval data. To compare pre-deployment Health Risk Assessment II (HRA II) results to post-deployment HRA II results], Chi-square will be used for categorical variables and either T-tests or Mann-Whitney U tests for measured variables to determine relationships. ANOVA Repeated Measures will be used to determine relationships for interval data with multiple time points (multiple medical visits/injuries) and Cochran Q.

**Progress:** This protocol was terminated due to time constraints on the physical therapists. This study may be resubmitted in the future.



## **Detail Summary Sheets**

Allergy/Immunology Service, Department of  
Medicine

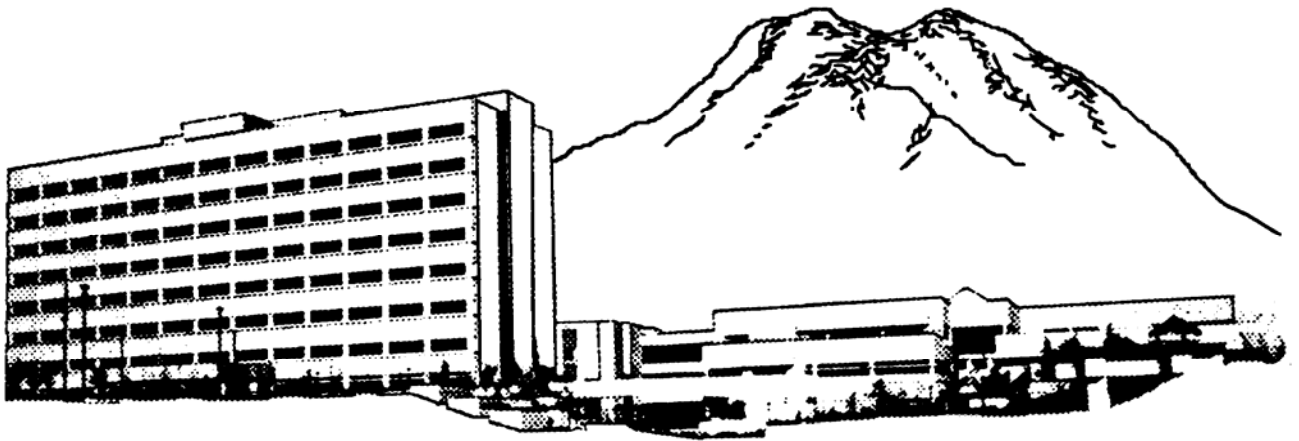
### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207061	<b>Status:</b> Completed
<b>Title:</b> Identification of Patients Prescribed B-blocker During Allergen Immunotherapy Without Allergist's Notification		
<b>Principal Investigator:</b> MAJ Ted Taiil Song, MC		
<b>Department:</b> Medicine/Allergy		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Linda L. Brown, MC		
<b>Start - Completion:</b> 12 Feb 2007 - Apr 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to perform a secondary analysis of a retrospective chart review to identify how many patients on Allergen immunotherapy (AIT) is concurrently prescribed B-blocker (BB) medication.

**Technical Approach:** Patients taking BB while on allergy shots is a relative contraindication. These patients can have more severe life threatening allergic reactions if they are taking BB while getting allergy shots. In addition, medications to treat this reaction do not work as well if patients are on BB. This study is to identify those patients who have been prescribed BB. Not all patients are aware of the BB medications and not know that they are taking it. By reviewing CHCS, we will be identifying those patients who have been prescribed BB. Then these patients will be evaluated by an allergist to see if they truly need to be on BB or can take an alternate medication, if possible. Study results will identify how many of patients are taking BB without notifying the allergy staff.

**Progress:** This protocol was reported as completed 24 October 2007, with 541 subjects (197 males and 254 females) receiving AIT identified. **RESULTS:** Based on 541 subjects receiving AIT, 10 (2.2%) females were prescribed alpha-blockers ( $p=0.003$ ). No males were identified in this category. In addition, 8 (1.8%) patients were simultaneously taking alpha-blockers while receiving AIT ( $p=0.01$ ). **CONCLUSION:** There are patients receiving AIT and taking alpha-blockers without notifying their allergist. This may lead to higher risk for more serious anaphylaxis.



## **Detail Summary Sheets**

Cardiology Service, Department of Medicine

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207068	<b>Status:</b> Terminated
<b>Title:</b> Randomized, multinational, double-blind study comparing a high loading dose regimen of clopidogrel versus standard dose in patients with unstable angina or non-ST segment elevation myocardial infarction managed with an early invasive strategy (OASIS 7)		
<b>Principal Investigator:</b> MAJ Kurt G. Kinney, MC		
<b>Department:</b> Medicine/Cardiology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL David T. Schachter, MC; MAJ Jason L. Davis, MC		
<b>Start - Completion:</b> 19 Apr 2007 - May 2010	<b>Funding:</b> Sanofi Aventis via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective is to determine whether a high dose regimen of clopidogrel (600 mg loading dose followed by 150 mg once daily for 7 days then 75 mg once daily) is superior to a standard dose of clopidogrel (300 mg loading dose followed by 75 mg daily) in preventing the composite of: (first co-primary endpoint) cardiovascular death, MI or stroke at 30 days (second co-primary endpoint) cardiovascular death, MI, stroke or recurrent ischemia at 30 days), in patients with non-ST segment elevation acute coronary syndromes (ACS) who are treated with an intent to perform PCI as early as possible within 24 hours of randomization. Another objective is to determine whether a high dose of acetylsalicylic acid (ASA) is superior to a low dose of ASA in preventing the composite of cardiovascular death, MI, stroke or recurrent ischemia.

The secondary objectives are to evaluate the safety of clopidogrel high dose regimen compared to standard dose regimen in terms of major bleeding (i.e. severe bleeding and other major bleeding), and to evaluate the safety of ASA high dose regimen (300-325 mg) compared to low dose (75-100 mg) regimen in terms of major bleeding (i.e. severe bleeding and other major bleeding).

**Technical Approach:** This is a multinational, multicenter, randomized, 2x2 factorial design, parallel-group, double-blind study to study the safety and efficacy of high dose clopidogrel and ASA versus standard doses in the treatment of patients with non-ST segment elevation ACS with intent for PCI as early as possible within 24 hours of randomization. Subjects will be screened upon presentation to MAMC by the cardiology study staff. Consented subjects will be randomized and assigned to receive either standard dose clopidogrel (300 mg p.o. on day 1 followed by 29 days of 75 mg daily) or high dose clopidogrel (600 mg day 1 followed by 150 mg day 2-8, followed by 75 mg day 9-30). All subjects will receive high dose ASA on day 1 (300 mg) then randomly be assigned to standard dose (75-100 mg daily) or high dose 300-325 mg daily. Subjects will be followed for safety and efficacy through day 30.

**Progress:** This protocol was initially approved by the IRB on 27 February 2007; however, contract negotiations between the study sponsor and the HMJF failed and the protocol was terminated on 4 April 2007, prior to receiving final approval.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 201300	<b>Status:</b> Ongoing
<b>Title:</b> Jostent Coronary Stent Graft (HUD)		
<b>Principal Investigator:</b> COL David T. Schachter, MC		
<b>Department:</b> Medicine/Cardiology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.; MAJ Bruce R. Kenwood, MC		
<b>Start - Completion:</b> 25 Sep 2001 - Sep 2010	<b>Funding:</b> Jomed via HDE	<b>Periodic Review:</b> 28 Aug 2006

**Study Objective:** Humanitarian Use Device

**Technical Approach:** The Jostent Coronary Stent Graft is approved as an HUD for the indication of arterial perforation. Physicians trained to deploy the stent will be added as associate investigators upon receipt of documentation of training. Use of the device will be tracked per 21 CFR 814.124(a).

**Progress:** This Humanitarian Use Device was not utilized during FY07. A Jostent device was inserted in a patient for a perforated saphenous vein graft in April 2005, who continues to be followed.

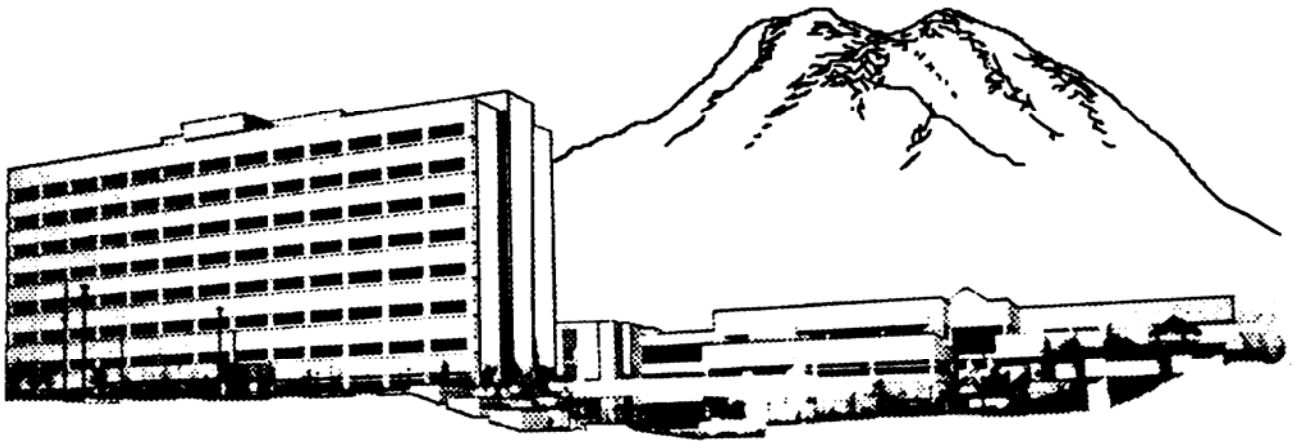
### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 202300	<b>Status:</b> Terminated
<b>Title:</b> CardioSEAL Septal Occlusion System (HUD)		
<b>Principal Investigator:</b> COL David T. Schachter, MC		
<b>Department:</b> Medicine/Cardiology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 11 Mar 2002 - Dec 2004	<b>Funding:</b> Nitinol Med Tech via HDE	<b>Periodic Review:</b> 24 Jan 2006

**Study Objective:** Humanitarian Use Device

**Technical Approach:** The CardioSEAL Septal Occlusion System is approved as an HUD for the indication of patent foramen oval closure (PFO). MAMC investigators trained to deploy this device must submit certificates of training and updated curriculum vitae to the Chairman, IRB. Use of the device will be tracked per 21 CFR 814.124(a).

**Progress:** The CardioSEAL was withdrawn as an HDE effective 31 October 2006. NMT was recently contacted by the FDA to review its existing HDE, which was approved more than six years ago. Since the HDE was approved, clinical conditions have significantly changed and the subset of patients who once qualified for consideration for PFO closure has increased beyond 4,000; the limit normally allowed under the HDE indication. The withdrawal does not reflect a device safety issue. CardioSEAL(R) will continue to be commercially available in the United States under the pre-market approval (PMA) indication for ventricular septal defects (VSD). No further use of the device occurred during the last approval period. Nine patients have undergone successful implantation of the CardioSEAL device without complications. All had strokes/TIA and evidence of PFO by bubble study. No further stroke/TIA events have been detected in any of the nine patients.



## **Detail Summary Sheets**

Hematology/Oncology Service, Department  
of Medicine

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 90027	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 8851 (EST 5811, INT-0101): Phase III Comparison of Combination Chemotherapy (CAF) and Chemohormonal Therapy (CAF + Zoladex or CAF + Zoladex + Tamoxifen) in Premenopausal Women with Axillary Node-Positive, Receptor- Positive Breast Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 16 Feb 1990 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 5 Dec 2007

**Study Objective:** To compare the recurrence rates, disease-free intervals, relative toxicities, and hormone-receptor-positive survival for premenopausal women with axillary lymph node-positive breast cancer given adjuvant therapy with combination chemotherapy using cyclophosphamide, doxorubicin, and 5-FU (CAF) alone or CAF followed by Zoladex, or CAF followed by Zoladex plus Tamoxifen; and to assess the effect of CAF, CAF plus Zoladex, and CAF plus Zoladex and Tamoxifen on hormone levels (LH, FSH, and estradiol) in these patients.

**Technical Approach:** Patients will be nonpregnant females who have undergone excision of the primary breast tumor mass, proven histologically to be invasive breast adenocarcinoma and must have one or more pathologically involved axillary nodes. Patients who undergo total mastectomy may receive post-operative radiotherapy at the discretion of the investigator. Patients who have had prior hormonal therapy or chemotherapy for breast cancer are ineligible. Patients will be randomized to CAF alone for six cycles or to CAF for 6 cycles followed by monthly Zoladex for 5 years, or to CAF for 6 cycles followed by daily Tamoxifen and monthly Zoladex for 5 years. Adjuvant therapy will be instituted as soon as possible after mastectomy or lumpectomy. The interval between definitive surgery and initiation of adjuvant chemotherapy will not be >12 weeks. When planned, radiation therapy may be administered prior to or after (within 4 weeks of) completion of 6 cycles of adjuvant chemotherapy.

**Progress:** This protocol closed enrollment in February 1994, with six subjects enrolled. Three subjects are deceased and three remain disease free and continued to be followed at MAMC during FY07. No adverse events or changes to the protocol were reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 91094	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S9007 (ECOG S9007), Cytogenetic Studies in Leukemia Patients		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 7 Feb 1992 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 22 Jan 2008

**Study Objective:** (1) To estimate the frequencies and prognostic significance of cytogenetic abnormalities in marrow or blood cells of leukemia patients prior to treatment on Southwest Oncology Group protocols and at various times in the course of their treatment, (2) To estimate correlations between the presence of cytogenetic features and of clinical, pathophysiological, cellular, or molecular characteristics in these patients and (3) To provide quality control for all Southwest Oncology Group cytogenetic data.

**Technical Approach:** This is a companion protocol for all Southwest Oncology Group leukemia protocols. Bone marrow or peripheral blood specimens will be forwarded to a SWOG referral cytogenetics laboratory (Oregon Health Sciences University, Portland, Oregon is the nearest to Madigan Army Medical Center). The referral lab will return a cytogenetics report to MAMC. Specimens will be collected as outlined in each individual leukemia protocol.

**Progress:** This laboratory protocol remains open to enrollment, with one subject enrolled at MAMC. Revision #32 and #33 changes to the protocol and the addition of an associate investigator were submitted and approved at the time of this report.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 93032	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9061 (EST-2190, INT 0121): A Phase III Study of Conventional Adjuvant Chemotherapy vs High Dose Chemotherapy and Autologous Bone Marrow Transplantation or Stem Cell Transplantation as Adjuvant Intensification Therapy Following Conventional Adjuvant Chemotherapy in Patients with Stage II and III Breast Cancer at High Risk of Recurrence		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 7 Oct 1993 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 13 Nov 2007

**Study Objective:** To compare the sites and rates of recurrence, disease-free survival and overall survival, and toxicity of adjuvant chemotherapy (CAF) with adjuvant chemotherapy plus high-dose therapy with cyclophosphamide and the TEPA with autologous marrow infusion in patients with breast cancer with 10 or more positive lymph nodes.

**Technical Approach:** Patients will be stratified according to estrogen receptor status, age, and menopausal status and then randomized to receive radiotherapy plus tamoxifen or high-dose chemotherapy and autologous bone marrow transplantation. Both arms will receive cyclophosphamide 100 mg/m<sup>2</sup> PO X 14 days, doxorubicin 30 mg/m<sup>2</sup> IV days 1 & 8, and flurouracil 500 mg/m<sup>2</sup> IV days 1 & 8 repeated every 28 days x 6 cycles (CAF). Patients receiving CAF without bone marrow transplantation will begin radiation therapy within 4 weeks of the last dose of chemotherapy or when the WBC > 2900 and Platelets > 100,000. Patients randomized to receive high-dose chemotherapy will have bone marrow harvested no sooner than 4 weeks nor longer than 8 weeks after the last previous dose of myelotoxic chemotherapy. The CBC must be normal and the bone marrow normocellular and free of tumor by bilateral iliac crest biopsy within 4 weeks prior to storage. After the bone marrow is harvested, high-dose chemotherapy of cyclophosphamide 6000 mg/m<sup>2</sup>/96 hr and ThioTEPA 800 mg/m<sup>2</sup>/96 hr (4 days), will be given by continuous infusion over 4 days, days -6 to -2. Autologous bone marrow reinfusion will be on day 0. Patients receiving BMT will again be randomized to receive GM-CSF as a daily 2, 6 or 24 hour intravenous infusion beginning 2-4 hours after bone marrow infusion. GM-CSF will be initiated at a dose of 250 mcg/m<sup>2</sup>/d. Treatment will continue until the patient has achieved an absolute neutrophil count (ANC) of = 1000 cells/ul on 3 consecutive days or a planned duration of 28 days of treatment.

Tamoxifen 20 mg PO q.d. will be given to all patients who are estrogen or progesterone receptor positive after the completion of all chemotherapy for 5 years. For patients not randomized to receive transplant, Tamoxifen should be initiated 28 days after the start of the last CAF cycle. Patients randomized to receive transplant should begin Tamoxifen following transplant when WBC > 4000 and/or ANC > 2000. Patients will be taken off-study if there is development of metastatic disease at any time while therapy is ongoing. Measurement of effect is recurrence, disease-free survival or survival (survival is measured from the date of randomization to date of death). At measured times during the study a Breast Chemotherapy Questionnaire (BCQ) will be completed to separately document the changes in psychosocial function that occur on the two regimens. Not all subjects will complete the questionnaire at all time points, but if at least 150 per arm have complete data, the width of a 95% confidence interval on the mean change in scores would be about  $\pm 0.09$ . The BCQ will also be used to make comparisons between regimens. A 2 degree of freedom test based on the difference of the means of the 36 week evaluation and the difference of the means of the 52 week evaluation will be used.

**Progress:** This protocol closed enrollment in August 1998, with one subject enrolled who remains disease free and continued to be followed at MAMC during FY07. No adverse events or changes to the protocol were reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 93097	<b>Status:</b> Terminated
<b>Title:</b> SWOG 9205: Central Prostate Cancer Serum Repository Protocol		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 7 May 1993 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 10 Apr 2006

**Study Objective:** 1) To store serum of patients with confirmed adenocarcinoma of the prostate entered onto clinical trials conducted by the SWOG Genitourinary Committee. 2) To provide the serum of the above patients entered onto SWOG studies for specific clinical-laboratory investigations outlined on separate SWOG protocols approved by the Genitourinary Committee Tumor Biology Subcommittee.

**Technical Approach:** This serum bank is to provide the opportunity for study of new or existing markers or other tests in a prospective or retrospective fashion, in order to test their usefulness as diagnostic or management tools in prostate cancer at all stages. Specific information regarding the nature of individual tests to be conducted on the serum samples of these patients will be described in individual protocols. All serum samples (approx. 3 - 5 cc) will be collected from patients in the frequency and timing indicated on specific protocols. Samples will be spun 15 minutes after collection and stored at a minimum of -20°C. Samples will be frozen and shipped to the Serum Bank Coordinator.

**Progress:** This protocol was permanently closed by SWOG in October 2006, discontinuing long term follow-up reporting requirements for fourteen subjects enrolled at MAMC. A central laboratory is now being used for all specimen submissions.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 93136	<b>Status:</b> Completed
<b>Title:</b> SWOG 9221, MDACC ID 91-025, INT-191-001: Phase III Double-Blind Randomized Trial of 13-Cis Retinoic Acid (13-cRA) to Prevent Second Primary Tumors (SPTs) in Stage I Non-Small Cell Lung Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 2 Jul 1993 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 24 May 2006

**Study Objective:** To evaluate: (1) the efficacy of 13-cis-retinoic acid (13-cRA) in reducing the incidence of SPTs in patients who have been treated for Stage I non-small cell lung cancer with complete surgical resection; (2) the qualitative and quantitative toxicity of 13-cRA in a daily administration schedule; and (3) compare the overall survival of patients treated with 13-cRA vs. patients treated with placebo.

**Technical Approach:** Patients enrolling into this study will be stratified according to histology, T stage and smoking status then registered into a Single-Blind, 8 week run-in period to test compliance. All patients will receive placebo during this period. After Run-in the patients will be randomized into a double-blind trial to receive 13-cRA (30 mg p.o./d x 3 yrs vs. Placebo (30 mg p.o./d x 3 yrs). Each group will have a 4 year follow-up period.

The final analysis will be undertaken shortly after seven years. The primary hypothesis for the study is whether 13-cRA lowered the rate of second primary tumors (SPT). All patients randomized will be grouped according to the assigned treatment. Patients who are either purely lost to follow up or died without a SPT occurring will be included in the actuarial analysis with a censored status on the last day of contact. The primary hypothesis of treatment benefit will be tested using the proportional hazards model.

**Progress:** This protocol was permanently closed by SWOG in June 2007, discontinuing long term follow-up reporting requirements. The protocol closed enrollment in April 1997, with eight subjects enrolled; five subjects remained disease free.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 93166	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9303: Phase III Study of Radiation Therapy, Levamisole, and 5-Fluorouracil versus 5-Fluorouracil and Levamisole in Selected Patients With Completely Resected Colon Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 5 Nov 1993 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 2 Aug 2007

**Study Objective:** To determine whether 5-FU, levamisole and radiation therapy results in superior overall survival when compared to 5-FU and levamisole without radiation therapy in the management of patients with completely resected pathologic stage T4BN0-2 colon cancer and selected patients with T3N1-2 colon cancer.

**Technical Approach:** This randomization clinical trial will compare radiation therapy, 5FU and levamisole with 5FU and levamisole in patients with completely resected colon cancer at high risk for local-regional recurrence and limited risk for system disease.

We will compare 5FU and levamisole, as delivered in the prior intergroup study, with one month of 5FU and levamisole followed by 5-5 1/2 weeks of 5FU, levamisole, and local-regional RT (45-50.4 Gy in 25-28 fractions), followed by 43 weeks of 5FU and levamisole.

**Progress:** This protocol closed enrollment in December 1996, with one subject enrolled who remains disease free and continued to be followed at MAMC during FY07. No adverse events or changes to the protocol were reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 94163	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9410 (INT 0148): Doxorubicin Dose Escalation, With or Without Taxol, As Part of the CA Adjuvant Chemotherapy Regimen for Node Positive Breast Cancer: A Phase III Intergroup Study		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 20 Jan 1995 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 16 Aug 2007

**Study Objective:** To determine (1) whether dose escalation of doxorubicin used as an adjuvant with cyclophosphamide in patients with early breast cancer will increase disease free and overall survival; (2) whether the use of Taxol as a single agent after the completion of 4 cycles of cyclophosphamide and doxorubicin in combination will further improve disease-free and overall survival compared to cyclophosphamide and doxorubicin alone; (3) if Taxol following standard dose cyclophosphamide and doxorubicin will be as effective or more effective than high dose cyclophosphamide and doxorubicin without Taxol; (4) to access the toxicity of the different doses of cyclophosphamide and doxorubicin with and without Taxol using the end point of life threatening or lethal toxicity; (5) whether the longer duration of chemotherapy treatment for patients randomized to receive Taxol is associated with a reduction in local recurrence in patients with lumpectomy and radiotherapy.

**Technical Approach:** Women with breast cancer, who have been treated with either mastectomy or segmentectomy will receive adjuvant chemotherapy. All patients will receive 4 courses of cyclophosphamide and doxorubicin (21 day cycle), but the doxorubicin dose will vary depending upon the randomization. Patients randomized to high dose doxorubicin will also receive G-CSF & ciprofloxacin. Some women will be randomized to receive Taxol after 4 cycles of AC chemotherapy is completed. They will receive taxol day 1 of a 21 day cycle for 4 cycles. Women with ER positive tumors will be given tamoxifen for 5 years.

**Progress:** This protocol closed enrollment in April 1997. Past reports stated that nine subjects were enrolled; however, this information was corrected reporting that only six subjects enrolled. Four subjects remain disease free and continued to be followed at MAMC during FY07. Two have died due to progressive disease.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 95003	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9401: A Controlled Phase III Evaluation of 5-FU Combined with Levamisole and Leucovorin as Surgical Adjuvant Treatment Following Total Gross Resection of Metastatic Colorectal Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 18 Nov 1994 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 4 Oct 2007

**Study Objective:** To determine in patients who have undergone complete gross surgical resection of metastatic colorectal cancer whether postoperative adjuvant chemotherapy with a new regimen of 5-fluorouracil (5-FU) plus leucovorin plus levamisole will result in improved survival compared to postoperative adjuvant chemotherapy with a standard 5-FU plus levamisole regimen.

**Technical Approach:** Patients will be randomly selected to treatment Arm I or treatment Arm II. Arm I consists of the standard regimen of 5-FU given by rapid intravenous infusion for 5 consecutive days, plus levamisole given by mouth three times daily for three consecutive days every other week for one year. Arm II is a new chemotherapy regimen which adds leucovorin in addition to the 5-FU and levamisole. 5-FU and leucovorin are given by rapid intravenous injection for five consecutive days every four to five weeks for one year. Levamisole is given by mouth three times per day for three days in a row every two weeks during the first two months, then every 2-3 weeks for a total of one year.

**Progress:** This protocol closed enrollment in September 1996, with one subject enrolled who remains disease free and continued to be followed at MAMC during FY07. No adverse events or changes to the protocol were reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 95093	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9402: Phase III Intergroup Randomized Comparison of Radiation Alone vs Pre-Radiation Chemotherapy for Pure and Mixed Anaplastic Oligodendrogliomas		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 19 May 1995 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 12 Feb 2007

**Study Objective:** 1) overall survival 2) compare time to tumor progression between the two arms 3) the frequency of severe (= grade 3) toxicities will be examined. 4) compare quality of life and neurologic function between the two arms. 5) identify the key histopathologic criteria necessary to make the diagnosis of anaplastic oligodendroglioma and mix oligo-astrocytoma; evaluate the diagnostic and prognostic relevance of chromosomal alterations; evaluate the diagnostic and prognostic relevance of DNA ploidy and indices of proliferation including percent S and percent G2M; study the diagnostic and prognostic relevance of immunohistochemical markers of cellular function and/or glial development; and evaluate the transnational relevance of tumor suppressor genes and oncogenes.

**Technical Approach:** This is a non-blinded randomized intergroup study and is different from other randomized trials for malignant glioma in three respects. First, it will evaluate the role of adjuvant chemotherapy in a recognizable subset of patients with malignant glioma, those with oligodendroglial differentiation. Second, the RT treatment volume will be based on a postoperative pre-randomization MR image, rather than the customary preoperative diagnostic CT or MR. Third, in the experimental arm of this study, chemotherapy will be given prior to RT. Patients whose tumors progress on chemotherapy will proceed to RT immediately. There will be a central pathology review prior to randomization, central radiology review to assess response to PCV and to substantiate tumor progression, and a quality of life assessment (QLA) to document the acute and chronic toxicities of chemotherapy and radiation including effects on cognitive function. Surgery and radiotherapy  $\pm$  PCV may adversely affect a patient's physical and emotional functioning. The Karnofsky performance status (KPS) will measure physical well-being. To complement KPS, the Mini-Mental Status exam (MMSE) will be administered to patients to assess cognitive ability. Assessment of differences in quantitative survival will be performed between the two therapeutic regimens supplemented with qualitative survival by the assessment of KPS, MMSE, and QLA.

**Progress:** This protocol closed enrollment in March 2002, with one subject enrolled who remains disease free and continued to be followed at MAMC during FY07. No adverse events or changes to the protocol were reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 96095	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9514: Phase III Double-Blind, Placebo-Controlled, Prospective Randomized Comparison of Adjuvant Therapy with Tamoxifen vs. Tamoxifen & Fenretinide in Postmenopausal Women with Involved Axillary Lymph Nodes and Positive Receptors, Intergroup		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 21 Jun 1996 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 26 Mar 2007

**Study Objective:** 1) To compare disease-free survival and overall survival of postmenopausal primary breast cancer patients with involved axillary nodes and positive estrogen or progesterone receptors who are treated with standard adjuvant tamoxifen vs. tamoxifen and fenretinide; 2) to gain wider experience and toxicity information on the combination of tamoxifen and fenretinide; and 3) to obtain tumor tissue from these patients for future biologic studies of relevance to this patient population.

**Technical Approach:** The present standard of therapy for node positive and ER positive post menopausal women is Tamoxifen alone. There are some studies that suggest that the addition of adjuvant chemotherapy combined with hormonal therapy will prolong relapse free and overall survival. However, not all patients, especially in the over 65 year old age group, can tolerate or want the significant side effects of chemotherapy. Thus, a less toxic regimen is needed. This study attempts to use a chemoprophylactic approach along with the standard Tamoxifen treatment for this group of patients. This new retinoid has shown some effectiveness in Phase I and II studies when given in combination with Tamoxifen to untreated metastatic breast cancer patients. This study will test its use in a Phase III randomized, prospective, placebo-controlled trial. The side effects seem to be fairly minimal except for night blindness which will be closely monitored during this trial.

**Progress:** This protocol closed enrollment in November 1999, with four subjects enrolled who remain disease free and continued to be followed at MAMC during FY07. No adverse events or changes to the protocol were reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 96118	<b>Status:</b> Completed
<b>Title:</b> SWOG 9515: Phase III Intergroup Trial of Surgery Followed by (1) Radiotherapy vs. (2) Radiochemotherapy for Resectable High Risk Squamous Cell Carcinoma of the Head and Neck		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 20 Sep 1996 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 10 Apr 2006

**Study Objective:** 1) To determine the efficacy of concurrent cisplatin and radiotherapy following surgical resection in patients who have advanced squamous cell carcinoma of the head and neck region; 2) to test whether the use of concurrent chemoradiotherapy following surgery increases locoregional control rates; 3) to determine if the patterns of first failure are changed by the use of concurrent chemotherapy; 4) to determine whether the use of concurrent chemoradiotherapy prolongs disease-free survival and/or overall survival; and 5) to compare the toxicity of concurrent chemoradiotherapy versus radiation alone in the postoperative setting.

**Technical Approach:** In head and neck squamous cell carcinomas with high risk features, there is a 20 to 50 percent recurrence rate after surgical resection. These high risk features include greater than 2 lymph nodes positive, extracapsular extension of cancer in lymph nodes, and positive resection margins. In the past, patients with these high risk features had received radiation therapy for local control. There is evidence, however, that the addition of cisplatin with concurrent radiation therapy may help in local control. This data comes from in vitro as well as in vivo data showing cisplatin may be a radiation sensitizer that may have synergistic local effects on malignancies. The study is a Phase III randomized study that will compare standard radiation therapy against concurrent cisplatin and radiation therapy for resected squamous cell carcinoma of the head and neck. The added toxicities of neuropathy, nausea and emesis, renal failure, and bone marrow suppression are tolerable and can be prevented with medical measures. It is hoped that local recurrence will be reduced with this approach with minimal added toxicity.

**Progress:** This protocol was permanently closed by SWOG in March 2007, discontinuing long term follow-up reporting requirements for the one subject enrolled at MAMC who remained disease free.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 97070	<b>Status:</b> Ongoing
<b>Title:</b> SWOG JBR.10 (NCIC CTG BR.10): A Phase III Prospective Randomized Study of Adjuvant Chemotherapy with Vinorelbine and Cisplatin in Completely Resected Non-small Cell Lung Cancer with Companion Tumour		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 21 Mar 1997 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 23 Feb 2007

**Study Objective:** 1) To compare the duration of overall survival (OS) between completely rejected patients with T2 NO, T1-2N1 non-small cell lung cancer (NSCLC) who have received either adjuvant chemotherapy with vinorelbine and cisplatin or observation alone. 2) To determine disease-free survival. 3) To confirm the prognostic significance of ras mutations when present in the primary tumor. 4) To provide a comprehensive tumor bank linked to a clinical data base for the further study of molecular markers in rejected NSCLC. 5) To measure and compare health related quality of life in both treatment arms throughout the study period. 6) To evaluate toxicity related to chemotherapy.

**Technical Approach:** The role of adjuvant chemotherapy in Non-small cell lung cancer is controversial. Most clinical trials have shown no benefit to adjuvant chemotherapy. In the early 80's the lung cancer study group showed some benefit with combination chemotherapy in terms of survival, however, the control arm was not a strict observational arm and contained a "biological response modifier" in it. Thus with recent improved survival in Stage IV lung cancer shown compared to observation, it is assumed that using platinum based therapies may enhance survival in patients that have completely rejected non-small cell lung cancer. In patients with rejected Stage I, II, and III Non-small cell lung cancer it is known that the long term survival rates are 50 to 60%, 30 to 50%, and 19 to 49% respectively. It is thus the aim of this study to assess whether adjuvant therapy with Cisplatin and Vinorelbine will improve survival and relapse free survival compared to observation. In addition to the above study, tissue samples will be sent to the University of Washington for evaluation of Ras mutations to assess its prognostic importance.

**Progress:** This protocol closed enrollment in April 2001, with two subjects enrolled who remain disease free and continued to be followed at MAMC during FY07. No adverse events or changes to the protocol were reported.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 97096	<b>Status:</b> Completed
<b>Title:</b> SWOG 9059 (E1392, INT-0126): Phase III Comparison of Standard Radiotherapy versus Radiotherapy plus Simultaneous Cisplatin, versus, split-Course Radiotherapy plus Simultaneous Cisplatin and 5-Fluorouracil, in Patients with Unresectable Squamous Cell Carcinoma of the Head and Neck		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 16 May 1997 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 10 Apr 2006
<p><b>Study Objective:</b> 1) To compare the effectiveness of standard radiation therapy alone to radiation therapy and simultaneous chemotherapy with cisplatin to split-course radiation therapy with cisplatin and 5-fluorouracil infusion in patients with unresectable Stage III and IV squamous cell carcinoma of the head and neck. Endpoints will include complete response rate, time to treatment failure, and overall survival. 2) To compare the relative toxicities of these treatment arms, in this patient population. 3) To compare patterns of relapse or treatment failure among these regimens. 4) To further assess the role, timing, and success of surgery in patients achieving a response to non-operative therapy.</p> <p><b>Technical Approach:</b> Unresectable Squamous Cell Carcinoma has a dismal prognosis with 3 year survivals in the 25' range. Several studies have shown that adding chemotherapy to radiation therapy may improve response rates and may allow some patients to get surgery after therapy. There are two approaches to adding chemotherapy to radiation therapy. One way is to give concurrent therapy with Cisplatinum alone with combined continuous radiation therapy (Al Sarraf regimen) or to give combination Cisplatinum and 5-FU with split course (Adelstein Regimen). These two regimens have met with some success in single ARM Phase II studies and have resulted in some patients having subsequent surgeries translating into longer survivals. It is thus the aim of this study to evaluate efficacy of three different regimens with continuous radiation therapy alone serving as the third ARM. Toxicities from these regimens are reasonable.</p> <p><b>Progress:</b> This protocol was permanently closed by SWOG in January 2007, discontinuing long term follow-up reporting requirements. The protocol closed enrollment in April 2000, with two subjects enrolled at MAMC, one subject died of progressive disease.</p>		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 98112	<b>Status:</b> Ongoing
<b>Title:</b> SWOG C9581: Phase III Randomized Study of Adjuvant Immunotherapy with Monoclonal Antibody 17-1A Versus No Adjuvant Therapy Following Resection for Stage II (Modified Astler-Coller B2) Adenocarcinoma		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 20 Oct 1998 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 16 Aug 2007

**Study Objective:** (1) To determine whether adjuvant treatment with MoAb 17-1A will improve the probability of overall and disease-free survival, and increase disease-free intervals in patients who have undergone resection of a Stage II (pT3NO or pT4bNO) colon cancer, (2) to evaluate a panel of prognostic markers, in order to correlate these measures with survival and recurrence after adjuvant therapy in patients who have undergone resection of a Stage II (pT3NO or pT4bNO) colon cancer. The specific aims of the companion study will be: (a) to determine whether alterations in the expression of cell cycle related genes (thymidylate synthase, p53, and the cyclin-dependent kinase inhibitors p21 and p27) predict the risk of survival and recurrence in this patient population, (b) to determine whether alterations in markers of metastatic potential-expression of DCC and measures of tumor angiogenesis (microvascular density and vascular endothelial growth factor expression)-predict the risk of survival and recurrence in this patient population, (c) to determine whether a marker of cellular differentiation-sucrase isomaltase-predicts the risk of survival and recurrence in this patient population, and (d) to determine whether interactions among these tumor markers identify subsets of patients with significantly altered outcome.

**Technical Approach:** Subjects will be randomized and assigned to one of two treatment groups following standard surgical removal of their tumor. Group 1 will receive standard care which is surgery with no additional therapy after the tumor has been removed. Subjects will continue with routine check-ups, doctor visits and test. Group 2 will receive five antibody treatments using MoAb 17-1A. Subjects will receive the drug by as an intravenous infusion over a 2-hour time period once each 28 days. This 2-hour infusion will be repeated every 4 weeks for a total of 5 treatments. During treatment, various blood tests and x-rays will be used to determine whether the disease has returned. With subject's approval, tissue, body fluids, and other specimens obtained during the normal course of treatment will be forwarded to a special research laboratory for storage and scientific testing. Subjects will also be asked to complete a background information form to help define groups of patient being treated.

**Progress:** This protocol closed enrollment in May 2002, with one subject enrolled in FY98 who continued to be followed at MAMC during FY07. No adverse events or changes to the protocol were reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 99014	<b>Status:</b> Ongoing
<b>Title:</b> SWOG C9741: A Randomized Phase III Trial of Sequential Chemotherapy Using Doxorubicin, Paclitaxel, and Cyclophosphamide, or Concurrent Doxorubicin and Cyclophosphamide Followed by Paclitaxel at 14 or 21 Day Intervals in Women with Node Positive Stage II/IIIA Breast Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 26 Jan 1999 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 13 Nov 2007
<p><b>Study Objective:</b> (1) To compare sequential chemotherapy with Doxorubicin, Paclitaxel, and Cyclophosphamide to combined Doxorubicin and Cyclophosphamide followed by Paclitaxel for disease-free and overall survival, (2) to determine whether increasing the dose density of adjuvant chemotherapy (decreasing the interval between chemotherapy courses from 21 to 14 days) will improve disease-free and overall survival, and (3) to compare the toxicity for patients treated with sequential Doxorubicin, Paclitaxel, and Cyclophosphamide with toxicity for patients with concurrent Doxorubicin plus Cyclophosphamide followed by Paclitaxel at 14 and 21 day intervals.</p> <p><b>Technical Approach:</b> This is a randomized comparison of several aggressive combination chemotherapy regimens in the treatment of high-risk breast cancer due to positive lymph nodes. It compares the current standard of care for node positive breast cancer with several more aggressive variations. All patients will receive the same number of drugs and the same amount of drugs, but the order in which the drugs are given and the time between treatments (2 weeks versus 3 weeks) will be different. Arm 1, patients will receive Doxorubicin once every 3 weeks x 4 total doses followed by Paclitaxel once every 3 weeks x 4 total doses followed by Cyclophosphamide once every 3 weeks x 4 total doses. Arm 2, patient will receive Doxorubicin once every 2 weeks x 4 total doses followed by Paclitaxel once every 2 weeks x 4 total doses followed by Cyclophosphamide once every 2 weeks x 4 total doses. Arm 3, patients will receive Doxorubicin and Cyclophosphamide once every 3 weeks x 4 total doses followed by Paclitaxel once every 3 weeks x 4 total doses. Arm 4, patients will receive patients will receive Doxorubicin and Cyclophosphamide once every 2 weeks x 4 total doses followed by Paclitaxel once every 2 weeks x 4 total doses. G-CSF and Ciprofloxacin will be given concurrent with each arm to help ameliorate side effects of the treatments.</p> <p><b>Progress:</b> This protocol closed enrollment in March 1999, with three subjects enrolled. One subject is deceased and two continued to be followed at MAMC during FY07. No adverse events or changes to the protocol were reported.</p>		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 99019	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S9808: Long-Term Follow-Up Protocol: An Administrative Tool		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 20 Oct 1998 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 4 Oct 2007

**Study Objective:** To relieve the burden on Institutional Review Boards at Southwest Oncology Group Institutions for continuing review of protocols that are closed to patient registration, and on which no patients are currently receiving protocol treatment.

**Technical Approach:** When a study has been closed to patient accrual and patients have finished treatment, it still requires submission of data to the Southwest Oncology Group to report survival and remission status and occurrence of adverse events. On an annual basis, the Southwest Oncology Group Operations Office will notify the institutions as to which protocols are eligible for transfer to the Long Term Follow-Up protocol by periodically revising the list of applicable protocols. The institutional Principal Investigator or IRB will ultimately decide for the local institution whether the protocol should be included in this protocol or continue to be reviewed on its own. A report will be prepared and submitted for annual IRB review at individual institutions. This report will include title and date closed to patient entry.

**Progress:** No new protocols were added during FY07. As of September 2006, current protocols to be followed under this administrative tool are: 8516-1 patient; 8794-1 patient; 8809-2 patients; 9008-1 patient; 9035-1 patient; 9133-2 patients; 9304-1 patient; 9349-2 patients, 8814-3 patients; 8897-6 patients; 9313-1 patient.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 99040	<b>Status:</b> Ongoing
<b>Title:</b> SWOG JMA.17: A Phase III Randomized Double-Blinded Study of Letrozole Versus Placebo in Women with Primary Breast Cancer Completing Five or More Years of Adjuvant Tamoxifen		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 23 Feb 1999 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 27 Feb 2007

**Study Objective:** Primary: To determine the disease-free survival and overall survival (all cause mortality) for women who have previously received  $\geq 5$  years of adjuvant Tamoxifen, randomized to receive wither Letrozole 2.5 mg daily or placebo daily for 5 years.

Secondary: To evaluate the incidence of contralateral breast cancer. To evaluate the long term clinical and laboratory safety of Letrozole with special attention to: lipid profile as assessed by blood sampling (in a limited number of centers), cardiovascular morbidity and mortality (i.e. significant coronary heart disease, which includes myocardial infarctions and angina requiring percutaneous transluminal coronary angioplasty or coronary artery bypass graft, fatal and nonfatal strokes and all vascular deaths) as assessed by reported toxicity, the incidence of all bone fractures (with particular emphasis on hip and wrist fractures as indicators of osteoporosis) as assessed by reported toxicity, changes in bone density (in a limited number of centers), common toxicities as assessed by reported toxicity.

Third: To evaluate overall quality of life.

**Technical Approach:** This is a multi-centre, double-blind, placebo-controlled parallel randomized trial of the NCIC Clinical Trials Group, supported by Novartis. Patients will be stratified by: receptor status at diagnosis (positive, unknown), lymph node status at diagnosis (negative, positive, unknown), and a prior adjuvant chemotherapy (yes, no). Patients will be centrally randomized to receive one of the following treatments: Arm 1 (letrozole): 2.5 mg po daily x 5 years or Arm 2 (Placebo): po daily x 5 years.

**Progress:** This protocol closed enrollment in December 2005, with thirteen subjects enrolled; two continue to receive Letrozole. One subject died due to progressive disease, and twelve continued to be followed at MAMC during FY07. No adverse events or changes to the protocol were reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 99071	<b>Status:</b> Ongoing
<b>Title:</b> SWOG E2197: Phase III Study of Adriamycin/Taxotere vs. Adriamycin/Cytosan for the Adjuvant Treatment of Node Positive or High Risk Node Negative Breast Cancer			
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC			
<b>Department:</b> Medicine/Hematology & Oncology			<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC			
<b>Start - Completion:</b> 20 Jul 1999 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation		<b>Periodic Review:</b> 17 Apr 2007

**Study Objective:** To determine whether Adriamycin/Taxotere will improve disease-free survival and overall survival when compared to Adriamycin/Cytosan in lymph node positive (1-3 positive nodes) and high risk lymph node negative breast cancer. To compare toxicity of Adriamycin/Taxotere to Adriamycin/Cytosan.

**Technical Approach:** This is multi-site study with randomization to one of two arms: Adriamycin/Taxotere (AT) or Adriamycin/Cytosan (AC). The dosages for the AT group: Adriamycin 60 mg/M2 IV and Taxotere 60 mg/M2 IV over 1 hour infusion every 3 weeks x 4 cycles. Cipro 500 mg PO b.i.d. starting Day 8 and continuing x 10 days. If a patient is allergic to Cipro, an alternative broad spectrum antibiotic may be used. Decadron 8 mg PO b.i.d., beginning one day prior to treatment with Taxotere and continued for two additional days; repeat q 3 weeks x 4 cycles. The dosages for the AC group: Adriamycin 60 mg/m2 IV and Cytosan 600 mg/ml IV. Every 3 weeks x 4 cycles. In both groups, post-menopausal patients who are ER and/or PR positive will receive Tamoxifen 20 mg PO daily x 5 years at the completion of chemotherapy. G-CSF: Patients who have an episode of febrile neutropenia should be placed on G-CSF according to ASCO Guidelines. Patients who have febrile neutropenia after a subsequent dose of chemotherapy in spite of G-CSF should have the chemotherapy doses lowered by 25%.

**Progress:** This protocol closed enrollment in January 2000, with two subjects enrolled who continued to be followed at MAMC during FY07. No adverse events or changes to the protocol were reported.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 200036	<b>Status:</b> Ongoing
<b>Title:</b> SWOG E1199: A Phase III Study of Doxorubicin-Cyclophosphamide Therapy Followed by Paclitaxel or Docetaxel Given Weekly or Every 3 Weeks in Patients with Axillary Node-Positive Breast Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 29 Aug 2000 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 18 Dec 2007

**Study Objective:** (1) To determine whether docetaxel improves disease-free survival and overall survival when compared to paclitaxel following 4 cycles of doxorubicin-cyclophosphamide therapy (2) To determine whether weekly administration of taxanes (paclitaxel or docetaxel) for 12 weeks improves disease-free survival and overall survival when compared with the conventional (every 3 weeks) schedule for 4 cycles following 4 cycles of doxorubicin-cyclophosphamide therapy (3) To compare the toxicity of docetaxel given weekly for 12 weeks to that of paclitaxel given every 3 weeks for 4 cycles (4) To compare the toxicity of paclitaxel given weekly for 12 weeks for 4 cycles to that of docetaxel given every 3 weeks for 4 cycles (5) To compare the toxicity of paclitaxel given every 3 weeks for 4 cycles to that of docetaxel given every 3 weeks for 4 cycles and (6) To compare the toxicity of paclitaxel given weekly for 12 weeks to that of docetaxel given weekly for 12 weeks.

**Technical Approach:** This study compares aggressive chemotherapy schedules to standard of care for high risk node positive breast cancer. Eligible patients will be randomized into one of four treatment arms: Arm A, 12 weeks of Adriamycin and Cytoxan followed by 12 weeks of Taxol (the standard treatment); Arm B, 12 weeks of Adriamycin and Cytoxan followed by 12 weeks of Taxol (lower dose than standard); Arm C, 12 weeks of Adriamycin and Cytoxan followed by 12 weeks of Taxotere (medium dose); and Arm D, 12 weeks of Adriamycin and Cytoxan followed by 12 weeks of Taxotere (low dose).

All Arms will receive Adriamycin and cyclophosphamide, IV once every 3 weeks for 4 cycles. Then Arm A will receive Taxol, IV once every 3 weeks for 4 treatments. Arm B will receive Taxol IV once a week for 12 weeks of treatment. Arm C will receive Taxotere IV once every 3 weeks for 4 treatments. Arm D will receive Taxotere once a week for 12 weeks of treatment.

**Progress:** This protocol closed enrollment in January 2002, with fourteen subjects enrolled. One subject died due to progressive disease, and thirteen subjects remain disease free and continued to be followed at MAMC during FY07. No adverse events or changes to the protocol were reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 200040	<b>Status:</b> Ongoing
<b>Title:</b> SWOG E4494: Phase III Trial of CHOP versus CHOP and Chimeric Anti-CD20 Monoclonal Antibody (IDEC-C2B8) in Older Patients with Diffuse Mixed, Diffuse Large Cell and Immunoblastic Large Cell Histology Non-Hodgkin's Lymphoma		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 25 Jan 2000 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 18 Dec 2007

**Study Objective:** (1) To compare CHOP treatment with or without chimeric anti-CD20 monoclonal antibody (IDEC-C2B8) in elderly patients with diffuse mixed, diffuse large cell, and immunoblastic large cell non-Hodgkin's lymphoma of B lineage with respect to response rate, the time to treatment failure, toxicity and survival, (2) To compare IDEC-C2B8 monoclonal antibody as maintenance therapy to observation alone after CHOP chemotherapy with respect to time to treatment failure, duration of response, toxicity and survival after an initial response to induction therapy of CHOP + IDEC-C2B8, and (3) To determine if maintenance therapy with IDEC-C2B8 results in the conversion of any partial responses to a complete response.

**Technical Approach:** This study adds a new drug, chimeric anti-CD20 monoclonal antibody, to the standard treatment (cyclophosphamide, doxorubicin, vincristine and prednisone, CHOP) of Non-Hodgkin's Lymphoma. Patients eligible for this study will be randomized to receive or not to receive IDEC-C2B8 (anti-CD20) in conjunction with chemotherapy. Treatment Arm A, CHOP plus Anti-CD20 will receive the study drug IV over 6 to 12 hours on Days 7 and 3 before the first treatment cycle of CHOP. Anti-CD20 will also be given 48 hours prior to cycles 3, 5 and 7 of CHOP. Treatment Arm B will receive CHOP for a minimum of 6 or a maximum of 8 cycles. Restaging of disease after 4 cycles and again after 6 cycles will be done to determine response and eligibility to be randomized to Maintenance Treatment Arms C & D. Arm C will continue to receive Anti-CD20 IV, four weekly doses every 6 months for 2 years. Arm D will be the observation group.

**Progress:** This protocol closed enrollment in 2001, with two subjects enrolled. One subject died due to progressive disease, and the other subject continued to be followed at MAMC during FY07. No adverse events or changes to the protocol were reported.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 200084	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S9921: Adjuvant Androgen Deprivation versus Mitoxantrone plus Prednisone plus Androgen Deprivation in Selected High Risk Prostate Cancer Patients Following Radical Prostatectomy, Phase III		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 26 Sep 2000 - Jan 2002	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 22 May 2007

**Study Objective:** This study will evaluate overall survival using adjuvant systemic therapy in high risk localized prostate cancer patients following radical prostatectomy. Disease-free survival will also be evaluated. Patients will be randomized to one of the following two treatment arms: (A) Casodex, + Zoladex, (B) Novantrone/Prednisone followed by Casodex, + Zoladex. This study will also compare qualitative and quantitative toxicity between the two study arms.

**Technical Approach:** This study compares standard hormonal therapy after prostate cancer surgery to standard therapy plus chemotherapy to determine the best way to prevent relapse. Subjects will be randomized to receive either Treatment 1, Hormonal Therapy which consists of Zoladex, subcutaneous injection once every 12 weeks for two years or Treatment 2, Hormonal Therapy plus Mitoxantrone plus Prednisone which consists of Zoladex subcutaneous injection once every 12 weeks for two years, Casodex taken orally once a day for two years, Mitoxantrone, IV once every 21 days for 126 days (6 cycles) and Prednisone, taken orally twice a day for 126 days. Following study completion, subjects will be followed every 6 months for two years to assess response.

**Progress:** This protocol closed enrollment in January 2007, due to an increased risk of acute myelogenous leukemia seen in the study treatment arm. Fourteen MAMC subjects were enrolled. Personalized notification letters were approved by the IRB to alert patients to the new risk information, and included signs and symptoms to look for. Four subjects continue to receive treatment and all continue to be followed at MAMC during FY07. No adverse events were reported, and no further changes to the protocol were submitted beyond the addition of an associate investigator.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 200120	<b>Status:</b> Ongoing
<b>Title:</b> SWOG N9831: Phase III Trial of Doxorubicin and Cyclophosphamide (AC) Followed by Weekly Paclitaxel With or Without Trastuzumab as Adjuvant Treatment for Women with HER-2 Over-expressing or Amplified Node Positive or High-Risk Node Negative Breast Cancer (an Intergroup Study)		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 22 Aug 2000 - Dec 2005	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 2 Aug 2007

**Study Objective:** (1) To compare the combination AC followed by weekly paclitaxel with the sequential schedule of the combination of AC, weekly paclitaxel, and trastuzumab in terms of disease-free survival (DFS). (2) To compare the combination of AC followed by weekly paclitaxel with the combination of AC followed by the combination of weekly paclitaxel and trastuzumab in terms of DFS. (3) To compare the sequential schedule of AC, weekly paclitaxel, and trastuzumab with the combination of weekly paclitaxel and trastuzumab in terms of DFS. (4) To compare the cardiotoxicities of (a) AC followed by weekly paclitaxel, (b) AC followed by weekly paclitaxel followed by weekly trastuzumab, and (c) AC followed by weekly paclitaxel and trastuzumab followed by weekly trastuzumab.

**Technical Approach:** Subjects will be randomly assigned to one of three arms: Arm A - Adriamycin and Cytoxan (AC) by vein over about 30 minutes one day every three weeks for a total of four treatments. After all treatment with AC is done (about week 12), Taxol by vein over 1 hour one day every week for a total of 12 treatments. Total length of treatment will be about six months. Arm B - Subjects will be given Adriamycin and Cytoxan (AC) by vein over about 30 minutes one day every three weeks for a total of four treatments. After all treatment with AC is done (about week 12), you will get Taxol by vein over 1 hour one day every week for a total of 12 treatments. After all treatment with Taxol is done (about week 24), Herceptin by vein one day every week for one year. The first dose of Herceptin will be given over about 90 minutes. Subjects will be watched for 1 hour after the first dose of Herceptin. If they do well this first dose, other doses will be given over about 30 minutes. Total length of treatment will be about 18 months. Arm C - Subjects will be given Adriamycin and Cytoxan (AC) by vein over about 30 minutes one day every three weeks for a total of four treatments. After all treatment with AC is done (about week 12), subjects will be given Taxol, by vein over 1 hour, plus Herceptin, by vein one day every week, for a total of 12 treatments. After all treatment with Taxol plus Herceptin is done (about week 23), subjects will get Herceptin alone one day every week for six months. The first dose of Herceptin will be given over about 90 minutes. You will be watched for 1 hour after the first dose of Herceptin. If subjects do well this first dose, other doses will be given over about 30 minutes. Total length of treatment will be about one year.

Regardless of which treatment, at the end of all chemotherapy, subject may also get Tamoxifen, if estrogen or progesterone receptor positive, for five years. If subjects had a lumpectomy, they will also get radiation therapy after chemotherapy has ended. Blood samples will be taken before the start treatment for research use. Subjects will be followed indefinitely.

**Progress:** This protocol closed enrollment in April 2005, with nine subjects enrolled; eight continue to be followed per protocol. One subject's death was unrelated to study participation, two subjects were removed from the study due to decreases in LVF, but the remaining six completed study treatment. No adverse events or changes to the protocol were reported during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 201137	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S0012: A Comparative Randomized Study of Standard Doxorubicin and Cyclophosphamide Followed by Weekly Paclitaxel Vs. Weekly Doxorubicin and Daily Oral Cyclophosphamide Plus G-CSF Followed by Weekly Paclitaxel as Neoadjuvant Therapy for Inflammatory and Locally Advanced Breast Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 25 Sep 2001 - Oct 2004	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 21 Aug 2007
<p><b>Study Objective:</b> (1) To compare the microscopic pathologic response rates in patients with inflammatory and estrogen-receptor negative locally advanced breast cancer treated with weekly Doxorubicin and daily oral Cyclophosphamide given with G-CSF support to in-patients treated without "standard" Doxorubicin and Cyclophosphamide regimen given every three weeks, (2) To compare the toxicities of these two regimens, (3) To compare the delivered dose intensity of these two regimens, and (4) To assess the association between microscopic pathologic complete response and clinical complete response at the primary tumor site in these patients.</p> <p><b>Technical Approach:</b> This trial is designed to compare two different treatment regimens for breast cancer prior to surgery to see if one works better against breast cancer than the other in very poor risk patients who may benefit from up-front chemotherapy. The standard regimen of Adriamycin and Cyclophosphamide given Day 1 every 21 days is compared to a regimen of Adriamycin given once a week for 15 weeks and oral Cyclophosphamide daily for 15 weeks. Filgrastim and trimethoprim sulfa will also be given in this regimen to protect against toxicity of the chemotherapy agents used.</p> <p><b>Progress:</b> This protocol met accrual goals and closed enrollment in December 2005, with three subjects enrolled at MAMC. One subject is deceased and the other two continue to be followed per protocol. Revision #6 changes to the protocol was submitted and approved. No adverse events were reported.</p>		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 202010	<b>Status:</b> Ongoing
<b>Title:</b> SWOG E5597: Phase III Chemoprevention Trial of Selenium Supplementation in Persons with Resected Stage I Non-Small Cell Lung Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 23 Oct 2001 - Oct 2005	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 28 Aug 2007

**Study Objective:** (1) To evaluate the efficacy of selenium supplementation in reducing the incidence of second primary lung tumors in patients who have been treated for Stage I non-small cell cancer with complete surgical resection, (2) to evaluate the qualitative and quantitative toxicity of a selenium supplementation in a daily administration schedule and (3) to compare the incidence of specific cancers and mortality from cancer as well as overall survival of patients treated with selenium supplementation versus patients treated with placebo.

**Technical Approach:** Selenium chemo-prevention may improve upon patients with high risk of second lung primaries as well other aero digestive tract tumors.

**Progress:** This protocol remains open to enrollment with two subjects enrolled. One subject remains on study, but the other withdrew prior to leaving the area. No adverse events were reported. Update #4 changes to the protocol was submitted and approved.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 202012		<b>Status:</b> Ongoing	
<b>Title:</b> SWOG GO182: A Phase III Randomized Trial of Paclitaxel and Carboplatin Versus Triplet or Sequential Doublet Combinations in Patients with Epithelial Ovarian or Primary Peritoneal Carcinoma					
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC					
<b>Department:</b> Medicine/Hematology & Oncology				<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Jane Shen-Gunther, MC; LTC Tommy A. Brown, MC					
<b>Start - Completion:</b> 23 Oct 2001 - Nov 2004		<b>Funding:</b> SWOG via Henry M. Jackson Foundation		<b>Periodic Review:</b> 4 Oct 2007	
<b>Study Objective:</b> (1) To compare the efficacy of each experimental arm with the control arm (paclitaxel and Carboplatin). Efficacy will be determined through analysis of overall survival and progression-free survival, (2) To compare the response rate in patients with measurable disease, toxicities and complications of each treatment regimen and to describe dose-intensity and cumulative dose delivery for each regimen and (3) To extend the accrual into a study initiated with GOG Protocol #0172 which will assess whether inactivated BRCA1 and /or BRCA2 is a prognostic factor for clinical outcome.					
<b>Technical Approach:</b> This study is designed to compare the effectiveness and side effects of several chemotherapy combinations (Paclitaxel, Carboplatin, Gemcitabine, Topotecan, Doxil [Liposomal Doxorubicin]) which are known to be effective in women with ovarian or primary peritoneal cancer. This study will enroll adult females with histologic diagnosis of primary peritoneal carcinoma or epithelial ovarian carcinoma, Stage III or IV, with either optimal or suboptimal residual disease following initial surgery.					
<b>Progress:</b> This protocol closed to enrollment in September 2004, with eight subjects enrolled; three continued to be followed during FY07. No adverse events or changes to the protocol have been reported.					

### Detail Summary Sheet

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<b>Date:</b> 30 Sep 07	<b>Number:</b> 202074	<b>Status:</b> Ongoing
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**Title:** SWOG S9925 Lung Cancer Specimen Repository Protocol, Ancillary

**Principal Investigator:** MAJ Jasmine T. Daniels, MC

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**Department:** Medicine/Hematology & Oncology

**Facility:** MAMC

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**Associate Investigator(s):** MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC; MAJ Richard D. Reed, MC

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**Start - Completion:**  
24 Sep 2002 - Nov 2005

**Funding:**  
SWOG via Henry M. Jackson Foundation

**Periodic Review:**  
8 May 2007

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**Study Objective:** (1) To establish a central lung cancer specimen repository to serve as a resource for current and future scientific studies. (2) To utilize Southwest Oncology Group clinical database to perform clinic pathologic correlation with the results of those studies. (3) To test new hypotheses as they emerge.

**Technical Approach:** Patients enrolled into select other SWOG lung cancer studies will be asked to consent to this study as well. Tissue samples will be obtained and stored.

**Progress:** This protocol is a companion study to other SWOG lung cancer treatment trials and remains open to enrollment, with three subjects enrolled, none during FY07. All subjects are now deceased.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203084	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S0016, A Phase III Trial of CHOP + Rituximab vs. CHOP + Iodine-131-Labeled Monoclonal Anti-B1 Antibody (Tositumomab) for Treatment of Newly Diagnosed Follicular Non-Hodgkin's Lymphomas		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 29 Oct 2003 - Jul 2006	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 18 Jun 2007

**Study Objective:** (1) To compare progression-free and overall survival between CHOP-Rituximab vs. CHOPP+I-131 tositumomab. (2) To compare the response rate between CHOP-Rituximab vs. CHOPP+I-131. (3) To compare the toxicities of these two regimens. Also, to compare the molecular remission rates by measuring colonel rearrangements in the bone marrow at baseline and at one year post-treatment.

**Technical Approach:** This is a national trial with a goal accrual of 500 patients to determine if a radioisotope labeled Anti-CD20 antibody (tositumomab) added to standard CHOP chemotherapy is superior to a combination of CHOP plus the uncongealed anti-CD20 antibody Rituximab. Specifically the endpoints will include disease free survival, overall survival, response rate, rate of molecular remission and data will also be collected on the toxicity of therapy. Data analysis will be analyzed by the SWOG Data and Safety Monitoring Committee (DSMC). The power analysis by the SWOG DSMC includes a sample size of 250 per treatment arm will detect a response rate difference of 6% between treatments. Eligible subjects will be randomized into one of the two study arms. (1) CHOP chemotherapy plus the rituximab antibody, 6, 21 day treatment cycles or (2) CHOP chemotherapy followed by the I-131 anti-B1 antibody, tositumomab, 6, 21 day treatment cycles. Four to six weeks after completion of chemotherapy, subjects will receive treatment with by the I-131 anti-B1 antibody, tositumomab. Also, at the time of surgery, tumor tissue, tumor fluid, and blood will be collected and used for specific experimental molecular tests, called P53, PCNA, Apoptosis and Human tumor cloning assay.

**Progress:** This protocol remains open to enrollment, with three subjects enrolled who completed treatment. One subject is deceased due to progressive disease, and two remain in remission and continued on follow-up. No adverse events were reported. Amendment #4 & #5, Revision #8, #9 and #10, and the addition of an associate investigator were submitted and approved during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204034	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S0221, Phase III Trial of Continuous Schedule AC + G Vs. Q 2 Week Schedule AC, Followed by Paclitaxel Given Either Every 2 Weeks or Weekly for 12 Weeks as Post-Operative Adjuvant Therapy in Node-Positive or High-Risk Node-Negative Breast Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 26 Feb 2004 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 22 Jan 2008

**Study Objective:** (1) To compare the disease-free survival of patients with node-positive or high-risk node-negative breast cancer treated with the combination of doxorubicin and cyclophosphamide given every 2 weeks with Pegfilgrastim support with that of patients treated with weekly doxorubicin and daily oral cyclophosphamide with filgrastim support, with both treatments to be followed by paclitaxel given according to one of two schedules. (2) To compare the disease-free survival of patients with node-positive or high-risk node-negative breast cancer treated with either 12 weeks of weekly paclitaxel or paclitaxel given every 2 weeks with Pegfilgrastim support for 6 cycles following treatment with one of the two doxorubicin/cyclophosphamide regimens discussed above. (3) To compare the overall survival produced by the four treatment arms. (4) To compare the toxicity of the four treatment arms. (5) To examine the association of putative prognostic markers with outcome and the interaction of these markers with treatment.

**Technical Approach:** This is a 4-arm phase III randomized trial of two different dose-dense doxorubicin plus cyclophosphamide chemotherapy regimens followed by two different schedules of taxol administration used for the treatment of node positive and high risk node negative breast cancer. Major endpoints of the trial are disease free survival and overall survival with an anticipated accrual of 2000 patients per year for a goal of 4500 patients accrued over 2.2 years. The study DSMC will perform an interim analysis at years 2.5, 4 and 6.

**Progress:** This protocol remains open to enrollment, with a total of sixteen subjects enrolled. One subject is deceased and the other subjects continue to be followed per protocol. One internal event of Grade 4 neutropenia and extended hospitalization was reported. Amendment #4 and Revision #8 changes to the protocol and the addition of an associate investigator were submitted and approved during FY07.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204064	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S0230, Phase III Trial of LHRH Analog Administration During Chemotherapy to Reduce Ovarian Failure Following Chemotherapy in Early Stage, Hormone- Receptor Negative Breast Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; COL John B. Halligan, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 27 Jul 2004 - Apr 2009	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 26 Mar 2007

**Study Objective:** (1) To compare the rate of premature ovarian failure at two years following standard adjuvant chemotherapy with or without the addition of ovarian suppression with a LHRH analog during chemotherapy in premenopausal women with early stage, hormone-receptor negative breast cancer. (2) To compare rates of ovarian dysfunction at one year and two years following standard adjuvant chemotherapy with or without ovarian suppression and to evaluate ovarian reserve in the two groups at one and two years. In addition, this study will describe pregnancy and other fertility information in the two groups after treatment and during the five year follow-up period.

**Technical Approach:** This is a randomized national phase III trial comparing standard adjuvant chemotherapy with chemotherapy plus Goserelin in pre-menopausal women with Stage I, II or IIIA Estrogen receptor negative and progesterone receptor negative breast cancer. Suppression of ovarian function during chemotherapy with a LHRH analog has demonstrated high rates of ovarian preservation in small studies. Outcome variables include the rate of amenorrhea at the completion of chemotherapy, at one year and at two years following treatment. Serum levels of FSH, estradiol and inhibin B will also be obtained at these same time points. Fertility information to include the number of successful pregnancies and the number of miscarriages will be compared at one, two and five years after treatment. National accrual is 416 patients over three years of which an estimated 3 per year will be enrolled at MAMC.

**Progress:** This protocol remained open to enrollment during FY07, with no subjects enrolled at the time of this report. Revision #6 and #7 changes to the protocol and the addition of an associate investigator were submitted and approved. No external adverse events were reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204066	<b>Status:</b> Ongoing
<b>Title:</b> SWOG E2496: Randomized Phase III Trial of ABVD Versus Stanford V +/- Radiation Therapy in Locally Extensive and Advanced Stage Hodgkin's Disease With 0-2 Risk Factors		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; COL John B. Halligan, MC; LTC William B. Reece, MC		
<b>Start - Completion:</b> 17 Aug 2004 - Apr 2009	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 26 Mar 2007

**Study Objective:** 1) Compare the failure-free survival of patients with locally extensive or advanced Hodgkin's lymphoma treated with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) vs doxorubicin, vinblastine, vincristine, bleomycin, mechlorethamine, etoposide, and prednisone (Stanford V) with or without radiotherapy. 2) Compare the overall survival and freedom from progression in these patients at 5 and 10 years after treatment with these regimens. 3) Compare pulmonary function, incidence of second cancers, reproductive function, and deaths from causes other than Hodgkin's lymphoma in patients treated with these regimens.

**Technical Approach:** SWOG E2496 is a national intergroup randomized Phase III trial of two treatment regimens for the treatment of locally extensive and advanced stage Hodgkin's disease. Subjects with bulky disease will receive radiation therapy in addition to chemotherapy in the control ABVD treatment Arm and subjects with lymphoma masses > 5 cm will receive radiation therapy on the Stanford V Arm. The primary endpoint of the trial is failure free survival. Laboratory endpoints include relative risk of death and treatment failure in subjects with EBV-positive disease, the concordance between three different EBV detection techniques, and the relationship of EBV viral DNA clearance for the two treatment arms. Laboratory studies will also investigate the relationship between T-cell response and EBV status and the time course of the T-cell response. This is a national intergroup study expected to accrue 204 subjects per year for a total of 850 subjects. At MAMC 2 subjects per year are expected to enroll. Data and statistical analysis will be conducted by the sponsoring study group, ECOG (Eastern Cooperative Oncology Group) with planned interim analyses at 33% and 67% of the number of anticipated treatment failures. It is expected that 3 years of follow-up will be required after complete accrual.

**Progress:** This protocol closed enrollment in August 2006, with four subjects enrolled. One subject transferred to another facility and the remaining subjects continue to be followed. No changes to the protocol or adverse events were reported during FY07.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204094	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S0226, Phase III Randomized Trial of Anastrozole Versus Anastrozole and Fulvestrant as First Line Therapy for Post Menopausal Women With Metastatic Breast Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 29 Sep 2004 - Jun 2010	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 21 May 2007

**Study Objective:** (1) To compare time to tumor progression in post-menopausal women with metastatic breast cancer treated with Anastrozole versus Anastrozole and Fulvestrant. (2) To compare clinical benefit (CR, PR, confirmed or unconfirmed, or stable disease >24 weeks) and overall survival for this cohort of patients. (3) To assess the adverse events of Anastrozole as compared to Anastrozole and Fulvestrant in this cohort of patients. (4) To assess the prognostic significance of subtypes of ER positive and HER-2 status. (5) To assess parameters of estrogen and clinical pharmacology and estrogen levels as outlined in Sec. 15.4. (6) To compare the Anastrozole plasma levels on each treatment arm at 8 weeks, 16 weeks and 24 weeks after randomization.

**Technical Approach:** S0226 is a randomized Phase III trial of Anastrozole versus Anastrozole plus Fulvestrant as first line endocrine therapy for metastatic breast cancer. The end-points of the trial are to assess the time to tumor progression of each of these treatments, to assess response rates and to assess overall survival of patients. The trial will also assess the adverse effects of each treatment arm and the prognostic significance of tumor ER status and HER2 status. Pharmacokinetic data on Anastrozole plasma levels and serum estradiol levels will be measured in both treatment groups. The trial has a national goal accrual of 230 patients per year for 3 years, with a goal accrual of 5 patients per year here at Madigan. All data evaluation will be done through the SWOG. There will be a planned interim analysis of progression free survival after 50% and 75% of national goal accrual.

Patients will be randomized to receive either 1 mg Anastrozole by mouth every day or 1 mg Anastrozole orally every day and 250 mg of Fulvestrant intramuscular injection once every 28 days. This schedule will continue until disease worsens or side effects are unacceptable. Fulvestrant may be given if disease worsens and if other treatment is not required right away. The first fifty patients in each group will have blood drawn to measure drug levels.

**Progress:** This protocol remains open to enrollment with no patients enrolled at MAMC. Revision #1 and #2 changes to the protocol were submitted and approved. No external adverse events were reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204123	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S0106, A Phase III Study of the Addition of Gemtuzumab Ozogamicin (Mylotarg®) During Induction Therapy Versus Standard Induction With Daunomycin and Cytosine Arabinoside Followed by Consolidation and Subsequent Randomization to Post-Consolidation Therapy With Gemtuzumab Ozogamicin (Mylotarg®) or No Additional Therapy for Patients Under Age 56 With Previously Untreated DeNovo Acute Myeloid Leukemia (AML)		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 21 Mar 2005 - Jan 2012	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 23 Oct 2007
<p><b>Study Objective:</b> (1) To compare disease-free survival (DS) of patients under age 56 with previously untreated, de novo, non-M3, MAL who received gemtuzumab ozogamicin as post-consolidation therapy versus patients who received no post-consolidation therapy. (2) To compare the complete remission (CR) rate achieved by the addition of gemtuzumab ozogamicin to standard induction chemotherapy to that achieved with standard induction chemotherapy in patients under the age of 56 with previously untreated, de novo, non-M-3 AML. The durability of complete response will also be measured. (3) To estimate the frequency and severity of toxicities of the addition of gemtuzumab ozogamicin to induction therapy and post consolidation therapy. (4) To evaluate the prognostic significance of CD33 expression on the response rate of those patients who receive gemtuzumab ozogamicin. (5) To evaluate the prognostic significance of FLT3 mutations prior to therapy, and of minimal residual disease in remission specimens collected before and after consolidation therapy and after post-consolidation therapy with gemtuzumab ozogamicin. (6) To evaluate the prognostic significance of the flow cytometric detection of minimal residual disease in specimens collected before and after consolidation therapy and after post-consolidation therapy with gemtuzumab ozogamicin.</p> <p><b>Technical Approach:</b> This is a randomized phase III trial comparing standard induction chemotherapy for AML with or without the anti-leukemia monoclonal antibody Gemtuzumab ozogamicin (Mylotarg®). Patients will be further randomized for post-consolidation treatment with Gemtuzumab ozogamicin (Mylotarg®) versus no post-consolidation treatment. Due to enhanced toxicity in older patients, this trial is limited to adult patients less than age 56 at the time of study entry. The end points of the trial are to compare disease free survival, complete remission rates and to determine toxicities of each treatment Arm. The trial will also investigate the prognostic significance of CD33 expression, FLT-3 mutations, and the flow cytometric detection of minimal residual disease. The goal accrual of this trial is 684 patients over 5 years with an expected enrollment of 2 patients per year at MAMC.</p> <p><b>Progress:</b> This protocol remains open to enrollment with one subject enrolled at MAMC, now deceased due to fulminant and subsequently fatal damage to the liver assessed as a direct result of treatment with Mylotarg therapy. Appropriate changes to the consent form were approved, adding "severe injury to the liver (including but not limited to veno-occlusive disease or sinusoidal obstruction syndrome), which could be fatal" to the less-likely risks of Mylotarg. Revision #4 and #5 changes to the protocol were also submitted and approved.</p>		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205007	<b>Status:</b> Ongoing
<b>Title:</b> PSOC 2003: A Phase II Study Evaluating the Efficacy of Gemcitabine, Carboplatin, Dexamethasone and Rituximab for Previously Treated Lymphoid Malignancies, UW Protocol Number LYM.03.01		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC		
<b>Start - Completion:</b> 18 Feb 2005 - Oct 2009	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 23 Oct 2007

**Study Objective:** (1) To determine the feasibility and safety of Gemcitabine/Carboplatin/Dexamethasone with or without Rituximab in previously treated lymphoid malignancies. The primary end-point will be response rate (Rituximab will only be evaluated in CD20 positive malignancies). (2) To determine the efficacy of the above regimen. (3) To determine the ability to proceed to blood stem peripheral blood collection following the above regimens the impact of above regimen on stem cell reserve. (4) To determine remission duration.

**Technical Approach:** PSOC 2003 is a multicenter single arm phase II trial of Gemcitabine, Carboplatin, and Dexamethasone in the treatment of recurrent or refractory lymphoma (including B-cell, T-cell, and Hodgkin's disease). Patients with CD20 positive B-cell lymphoma will also be treated with Rituximab. The end points of the trial include response rate, duration of remission, and the ability to collect stem cells for possible future autologous stem cell transplant. The goal accrual of the study is 51 patients over 2 to 3 years. We anticipate accruing two patients per year at Madigan. The study will be monitored for accrual, adverse events and patient deaths every 6 months by the Study Investigator, Dr Ajay Gopal of the University of Washington and the Fred Hutchinson Cancer Research Center, and will be monitored annually by the Fred Hutchinson Cancer Research Center Protocol Data Monitoring Committee.

**Progress:** This protocol remains open to enrollment with two subjects enrolled, one during FY07. Both subjects have completed study treatment and continue to be followed. No adverse events have been reported. Amendment #5 and #6 changes to the protocol were submitted and approved.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205035	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S9910 Leukemia Centralized Reference Laboratories and Tissue Repositories, Ancillary		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 18 Mar 2005 - Feb 2010	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 22 Jan 2008

**Study Objective:** (1) To develop and apply laboratory assays for the rapid and precise diagnosis of leukemia patients and identify biologic, genetic, and molecular parameters that distinguishes different subtypes of human leukemia with differing responses to therapy. (2) To develop risk-adapted therapeutic approaches in which biologic, genetic, and molecular parameters are used to target individual patients to tailored therapeutic regimens, or, to randomize and stratify patients to different treatment arms of a therapeutic trial. (3) To develop new automated and standardized laboratory methods for the detection and monitoring of therapeutic responsiveness and minimal residual disease in leukemia patients and develop new clinical approaches to employ such data in therapeutic decision making and clinical trial design. (4) To maintain and expand tissue repositories of highly characterized leukemia samples from uniformly treated Southwest oncology Group patients to promote Intergroup and external fundamental scientific collaborations and to perform continued critical prospective and retrospective correlative biologic studies. (5) To utilize scientific information generated from Intergroup and collaborative studies to assist the leukemia committee in the development of new and more effective treatment regimens.

**Technical Approach:** The Southwest Oncology Group repositories are banks of extremely valuable leukemia samples which are made available to researchers who are studying various biological parameters and therapeutic diseases.

**Progress:** This tissue repository protocol remains open to enrollment with one subject enrolled during FY07.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206023	<b>Status:</b> Terminated
<b>Title:</b> A Multi-Center, Randomized, Phase 3 Study of Iodine I-131 Tositumomab Therapeutic Regimen Versus Ibritumomab Tiuxetan Therapeutic Regimen for Subjects with Relapsed or Transformed Follicular Non-Hodgkin's Lymphoma		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Antonio G. Balingit, MC; Jane E. Besich-Carter, BS, BCNP		
<b>Start - Completion:</b> 13 Apr 2006 - Jan 2011	<b>Funding:</b> GlaxoSmithKline via Henry M. Jackson Foundation	<b>Periodic Review:</b> 27 Mar 2007

**Study Objective:** This study will compare the proportion of subjects treated with Iodine I 131 tositumomab therapeutic regimen who experience any Grade 3/4 hematological adverse event with the proportion of subjects treated with ibritumomab tiuxetan therapeutic regimen who experience this type of adverse event. Subjects in this study must have had at least three prior therapies for either follicular non-Hodgkin's Lymphoma (NHL) or follicular NHL that has transformed to diffuse large cell lymphoma.

The secondary objectives for efficacy are comparison of the confirmed overall response rate, confirmed complete response rate, and duration of response, as well as event-free survival, progression free survival, time to next treatment, and overall survival between the two treatment groups. Establishment of the non-inferiority of Iodine I 131 tositumomab compared to ibritumomab tiuxetan based on event-free survival will be the principal secondary objective.

The secondary safety objectives are safety comparisons between the Iodine I 131 tositumomab and ibritumomab tiuxetan treatment groups for the following events: Infusional toxicities (all and Grade 3/4), Gastrointestinal toxicities (all and Grade 3/4), Immune response (Human Anti-Murine Antibody [HAMA]), Elevated thyroid-stimulating hormone (TSH), Myelodysplastic syndrome (MDS)/acute myelogenous leukemia (AML), Serious adverse events (SAEs) related to cytopenia (bleeding events, neutropenic, fever, infections, hospitalization for hematologic supportive care). To characterize the safety profile in the two treatment groups, including the frequency of adverse events, the duration of infusion, and tolerance of first subsequent NHL therapy. To summarize safety and efficacy outcomes during the first subsequent treatment encounter for NHL. To establish the non-inferiority of confirmed overall response rates and confirmed complete response rates between Iodine I 131 tositumomab and ibritumomab tiuxetan.

**Technical Approach:** This is a randomized, multi-center, Phase III study comparing I131 tositumomab (Bexxar) versus Y90 ibritumomab tiuxetan (Zevalin) in subjects with relapsed or transformed follicular non-Hodgkin's lymphoma who have received prior treatment with rituximab (Rituxan). A total of 350 subjects will be randomized into two treatment arms, with up to 10 subjects being enrolled at MAMC. Subjects will be randomly assigned to one of the two treatment arms. Randomization will be stratified by baseline bone marrow involvement, baseline blood count and prior fludarabine treatment and conducted separately within each stratum. Subjects on Arm A will be treated with the standard Zevalin regimen, including rituximab and radiolabeled ibritumomab tiuxetan in two separate doses for imaging and therapy. Subjects randomized to Arm B will be treated with the standard Bexxar regimen in two separate doses for imaging and therapy. Subjects in each arm will be followed for ten years after receiving study drug (five years for efficacy endpoints and ten years for safety endpoints). After study drug administration, labs will be drawn at least weekly for up to 13 weeks to closely monitor hematological toxicity. Response assessments will be done at Weeks 7, 13, 26, 39 and 52 during the first year, every six

months during the second year, then annually through five years or until first subsequent treatment. See schema, protocol page 22. The study is powered to detect a significant reduction of 15% in Grade 3/4 hematologic toxicity. In addition, the study will have 90% power to establish non-inferiority of the Bexxar treatment versus Zevalin.

**Progress:** This protocol was reported by the study sponsor as terminated in February 2007, due to enrollment issues and FDA review. No subjects were enrolled.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206068	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S0520: Phase II Study of PDX101 (NSC-726630) in Relapsed and Refractory Aggressive B-Cell Lymphomas		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 24 Jul 2006 - May 2011	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 8 Mar 2007

**Study Objective:** Primary objectives: (1) To evaluate response rate and toxicity in patients with relapsed and refractory aggressive B-cell lymphoma treated with this regimen. (2) To estimate the 6-month progression-free survival rate in patients with relapsed and refractory aggressive B-cell lymphoma with single agent PDX101 therapy. Correlative study objectives: (1) to assay the MHC Class II proteins (HLA-DR, DP, DQ), TUNEL and CD8 infiltration status by immunohistochemistry on paired pre- and post-treatment tumor samples for 20 patients on the enrolled, (2) to measure CIITA and HLA-DR mRNA expression using quantitative RT-PCR, and to explore in a preliminary manner the associations of these markers and progression-free survival and (3) to evaluate paired pre- and post-treatment peripheral blood mononuclear cells (PBMCs) from patient for histone acetylation conducted on pre- and post-needle core biopsies.

**Technical Approach:** This is a Phase II, open label, multi-site study of PDX101 in relapsed and refractory aggressive B-cell lymphoma. This study will enroll a total of 60 subjects (up to 3 at MAMC) with diffuse large, Burkitt's, Burkitt-like, primary mediastinal lymphoma. Patients will receive PDX101 at a dose of 1,000 mg/m<sup>2</sup>, as a 30 minute IV infusion, on Days 1-5 of a 21 day cycle. Nausea, vomiting, anemia, neutropenia and dehydration will be treated according to institutional standards. Diarrhea will be treated with loperamide. Treatment will be given on Days 1-5 of a 21 Day cycle. Physicals, laboratory tests and adverse event evaluation will be done prior to each subsequent cycle. Disease assessment will be done after Cycle 3, and then every 4 cycles until progression is documented. Patients will be removed from treatment after disease progression, symptomatic deterioration, unacceptable toxicity or completion of 2 years of treatment. Off-treatment evaluation will include monitoring for disease progression and survival for up to a total of 3 years. The primary goal of this study is to assess the response probability in patients with relapsed or refractory aggressive B-cell lymphoma treated with PDX101. Secondary endpoints will include toxicity, overall survival, time to treatment failure and time to progression. It is assumed that this therapy will be of no further interest if the true response probability is 5% or less, and of interest if the true response probability is 20% or more. The study has a two-stage design. If at least one of the first 20 patients responds, an additional 20 patients will be enrolled.

**Progress:** This greater than minimal risk protocol received final IRB approval 24 July 2006; no subjects enrolled during FY07. Study enrollment continues.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207054	<b>Status:</b> Ongoing
<b>Title:</b> CALGB 80101: Phase III Intergroup Trial of Adjuvant Chemoradiation after Resection of Gastric or Gastroesophageal Adenocarcinoma		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; MAJ Richard D. Reed, MC; LTC David E. McCune, MC; COL John B. Halligan, MC; MAJ Joseph P. Brooks, MC		
<b>Start - Completion:</b> 10 May 2007 - Mar 2012	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 2 Jan 2008

**Study Objective:** The primary objective of this study is to determine whether overall survival is prolonged in patients with surgically removed cancer of the stomach or esophageal-stomach junction who receive epirubicin, cisplatin, and continuous infusion of 5-FU (ECF regimen) before and after continuous infusion 5-FU plus radiation therapy when compared to those treated with short bolus 5-FU and Leucovorin before and after continuous infusion 5-FU plus radiation therapy.

Secondary objectives are to: determine whether disease-free survival as well as local and distant recurrence rates are prolonged in the ECF arm of the study when compared to the 5-FU/Leucovorin arm; prospectively assess the correlation of some prognostic tumor markers and features with overall survival and treatment-related toxicity; determine whether hospital procedure volume (at the center where surgery was performed) predicts recurrence-free and overall survival.

**Technical Approach:** This is a phase III, randomized, open label comparison of a standard regimen (Arm A) and an investigational regimen (Arm B) for resected gastric or gastroesophageal adenocarcinoma. Subjects will receive one 28-day cycle of chemotherapy, followed by a 5-week cycle of 5-FU infusion and radiation therapy. They will then have a 4 to 5 week rest period, then two more cycles of chemotherapy. The primary objective is overall survival. Secondary objectives of disease free survival and recurrence rates will be determined by annual CT scans after treatment is completed. This study also includes optional companion studies looking at tumor markers, specific germline polymorphisms and serum growth factor levels.

**Progress:** This greater than minimal risk protocol received initial approval by the IRB 23 January 2007, and final approval on 10 May 2007. Update #5 with administrative changes was submitted and approved during FY07. No patients have been enrolled.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207055	<b>Status:</b> Ongoing
<b>Title:</b> CTSU E5204, Intergroup Randomized Phase III Study of Postoperative Oxaliplatin, 5-Fluorouracil and Leucovorin vs. Oxaliplatin, 5-Fluorouracil, Leucovorin and Bevacizumab for Patients with Stage II or III Rectal Cancer Receiving Pre-operative Chemoradiation		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Richard D. Reed, MC; LTC David E. McCune, MC; COL John B. Halligan, MC; MAJ Joseph P. Brooks, MC		
<b>Start - Completion:</b> 10 May 2007 - Mar 2012	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 2 Jan 2008

**Study Objective:** The primary objective of this study is to compare the overall survival of patients with clinical Stage II and III rectal cancer who received pre-operative chemoradiation and were treated with oxaliplatin, leucovorin, and 5-fluorouracil with or without bevacizumab postoperatively. Secondary objectives are to (1) evaluate tolerance of treatment, patterns of cancer recurrence, and disease-free survival, (2) prospectively assess long-term rectal function, and long-term neurological side effects in these patients, (3) correlate certain molecular markers in tumor tissue with treatment effectiveness and survival, and determine the impacts of diabetes mellitus, body mass index (BMI), and weight gain on cancer recurrence and survival among this subset of patients.

**Technical Approach:** This is a Phase III study where patients with Stage II or Stage III Rectal cancer will be randomized to one of two treatments arms of FOLFOX-6, plus or minus Avastin. The outcomes will be overall survival rate and disease free survival.

**Progress:** This greater than minimal risk protocol received initial approval by the IRB 23 January 2007, and final approval on 10 May 2007. Multiple external adverse event reports were reviewed by the PI. Update #1 with administrative changes, and Addendum #2 with study eligibility and treatment clarifications were submitted and approved during FY07. No patients have been enrolled.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207067	<b>Status:</b> Ongoing
<b>Title:</b> CALGB 50303: Phase III Randomized Study of R-CHOP VS Dose-Adjusted EPOCH-R with Molecular Profiling in Untreated De Novo Diffuse Large B-Cell Lymphomas		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 16 May 2007 - Mar 2012	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objectives are to (1) compare the event-free survival of R-CHOP versus DA-EPOCH-R chemotherapy in untreated CD20+ diffuse large B-cell lymphomas, and develop a molecular predictor of outcome of R-CHOP and DA-EPOCH-R chemotherapy using molecular profiling.

The secondary objectives are to (1) compare the response rates, overall survival and toxicity of R-CHOP versus DA-EPOCH-R, (2) define the pharmacogenomics of untreated DLBCL and correlate clinical parameters (toxicity, response, survival outcomes and laboratory results) with molecular profiling, (3) assess the use of molecular profiling for pathological diagnosis, and (4) identify new therapeutic targets using molecular profiling.

**Technical Approach:** This is a phase III, randomized study of standard therapy (CHOP-R) versus an investigational regimen (dose adjusted EPOCH-R) for de novo diffuse large b-cell lymphoma. Patients with newly diagnosed DLBCL will be randomly assigned to either of the regimens, and receive up to 6 cycles of chemotherapy. Outcomes will be tracked with CT scans, laboratory data and adverse event information. Data will be compared between the two regimens on time to progression, survival and toxicity. A total of 478 subjects will be enrolled in the trial, with up to 8 subjects being enrolled at MAMC. Data will be collected and submitted to CALGB for final analysis. Ongoing information will be reviewed by a data safety monitoring board during the trial for safety and outcomes analysis. Final analysis will be presented by CALGB through publication and/ or abstract presentation.

**Progress:** This greater than minimal risk protocol was initially approved by the IRB on 27 February 2007, and received final approval 16 May 2007. Protocol Updates #3, #4, and #5 were submitted and approved by the IRB. No subjects enrolled during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 202043	<b>Status:</b> Completed
<b>Title:</b> CTSU RTOG 98-04: Phase III Trial of Observation +/- Tamoxifen vs. RT +/- Tamoxifen for Good Risk Duct Carcinoma In-Situ (DCIS) of the Female Breast		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 26 Feb 2002 - Feb 2005	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 9 Jan 2006
<b>Study Objective:</b> (1) Comparing whole breast radiation +/- Tamoxifen compared to wide excision to negative margins alone +/- Tamoxifen, in decreasing or delaying the appearance of local failure, both invasive and in situ, and preventing need for mastectomy, (2) assess distant disease free survival patients in either arm who fail with progression can be successfully salvaged with further definitive local therapy and adjuvant systemic therapy, (3) setting up a working pathology classification system for DECIS, (4) establishing an epidemiological questionnaire registry for companion studies of biomarkers, and (5) establish tissue bank of patients who progress to local failure in study breast.		
<b>Technical Approach:</b> To compare the efficacy of Tamoxifen with or without whole breast radiation, in decreasing or delaying the appearance of local failure, both invasive and in-situ, and preventing the need for mastectomy in women with ductal carcinoma in-situ (DCIS) of the breast.		
<b>Progress:</b> This protocol was closed by RTOG in July 2006, due to poor accrual. No patients enrolled at MAMC.		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 202083	<b>Status:</b> Completed
<b>Title:</b> A Randomized Phase III Trial of Gemzar versus Doxil with Crossover Treatment Option for Patients with Platinum-Resistant Ovarian, Fallopian Tube or Primary Peritoneal Cancer Undergoing Second or Third-Line Chemotherapy, Protocol Number: B9E-US-S301		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC		
<b>Start - Completion:</b> 14 Aug 2002 - Jul 2005	<b>Funding:</b> Lilly via Henry M. Jackson Foundation	<b>Periodic Review:</b> 16 Jul 2007

**Study Objective:** (1) To compare progression free survival in patients with platinum-refractory epithelial ovarian, Fallopian tube, or primary peritoneal carcinoma who have failed two or less prior regimens of chemotherapy that are treated with Doxil or Gemzar. (2) To compare response rate, duration of response, time to treatment failure, survival, and quality of life in patients with platinum-refractory epithelial ovarian, Fallopian tube, or primary peritoneal carcinoma who have failed two or less prior regimens of chemotherapy who are treated with Doxil or Gemzar.

**Technical Approach:** At MAMC there are expected to be 5-10 patients enrolled during approximately one year.

Patient screening will include written informed consent, medical history and demographics, tumor assessment by exam or imaging, FACT-O questionnaire, Zubrod Performance Status, LVEF, chemistry and hematology, CA-125 tumor marker, contraceptive status and serum pregnancy test. Patients on the Doxil arm will be treated with 50 mg/m<sup>2</sup> on Day 1 of each 28 day cycle. Treatment will continue for two cycles after a complete response, or until a cumulative maximum dose of 500 mg/m<sup>2</sup> has been given. Patients on the Gemzar arm will be treated with 1000mg/m<sup>2</sup> on Days 1 and 8 of a 21 day cycle. Treatment will continue for up to two cycles after complete response is attained. For patients with stable disease there is no maximum number of Gemzar cycles. Patients who have progressive disease may cross over to the other treatment arm if they are eligible. Patients will be monitored every cycle for toxicities, chemistry, hematology, performance status and CA-125 tumor staging. Dose adjustments will be made based on NCI toxicity criteria. FACT-O Quality of Life questionnaire will be administered every other cycle, and tumor assessment imaging will be performed every 12 weeks. Primary efficacy will be evaluated using Kaplan-Meier techniques. Secondary efficacy analysis will be conducted on response rate, duration of response, time to treatment failure, survival and quality of life. Response rates from the two treatment arms will be compared using Fisher's Exact test. Summaries on toxicity parameters will be provided.

**Progress:** This protocol closed enrollment in May 2004, with four subjects enrolled, all reported as deceased due to progressive disease. The protocol remained ongoing pending close-out of the database by the study sponsor during FY07, which was reported completed in September 2007.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 202088	<b>Status:</b> Completed
<b>Title:</b> CTSU E1A00 A Randomized Phase III Trial of Thalidomide (NSC #66847) Plus Dexamethasone versus Dexamethasone in Newly Diagnosed Multiple Myeloma		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 25 Jun 2002 - Jul 2005	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 21 May 2007

**Study Objective:** 1) To evaluate the response rate and toxicity of thalidomide plus dexamthasone and dexamethasone alone in patients with newly diagnosed myeloma. 2) To study the effect of thalidomide on bone marrow microvessel density and angiogenesis grade and on the expression of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) in the marrow.

**Technical Approach:** Compare a standard treatment for myeloma, dexamethasone to dexamethasone plus thalidomide. The goal of the study is to see if there is any difference between the two with respect to response rate, complications and quality of life or survival.

**Progress:** This protocol closed enrollment in April 2003, with one subject enrolled who withdrew from treatment after two cycles. The subject died of disease progression in November 2006, and the protocol was reported as completed in May 2007.

### Detail Summary Sheet

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<b>Date:</b> 30 Sep 07	<b>Number:</b> 202089	<b>Status:</b> Completed
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**Title:** CTSU CALGB 49907, A Randomized Trial of Adjuvant Chemotherapy With Standard Regimens, Cyclophosphamide, Methotrexate and Fluorouracil - (CMF) or Doxorubicin and Cyclophosphamide - (AC), Versus Capecitabine in Women 65 Years and Older with Node Positive or Node Negative Breast Cancer

**Principal Investigator:** LTC David E. McCune, MC

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<b>Department:</b> Medicine/Hematology & Oncology	<b>Facility:</b> MAMC
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**Associate Investigator(s):** MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; LTC Tommy A. Brown, MC

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<b>Start - Completion:</b> 5 Dec 2002 - Jul 2005	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 22 May 2006
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**Study Objective:** (1) To compare the effectiveness of standard chemotherapy (CMF or AC) with single agent Capecitabine with respect to disease-free survival in women 65 years and older with local and regional breast cancer. (2) To compare the effectiveness of standard chemotherapy regimens with Capecitabine with respect to overall survival.(3) To determine the effects of each treatment regimen on quality of life and physical function. (4) To assess the toxicity of each treatment program. (5) To study the adherence to an oral chemotherapy regimen in older patients.

**Technical Approach:** This study compares the oral anti-cancer drug Capecitabine to standard adjuvant therapy of Cyclophosphamide, Methotrexate and Fluorouracil, or Doxorubicin and Cyclophosphamide in women who have complete breast cancer surgery and are over 65 years old. The study will attempt to find a survival her forth difference in relapse rates or a quality of life.

**Progress:** This protocol met accrual goals and was closed by CALGB on 30 January 2007, with no MAMC subjects enrolled.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 202114	<b>Status:</b> Ongoing
<b>Title:</b> CTSU CALGB 40101, Cyclophosphamide and Doxorubicin (CA) (4 VS 6 Cycles) versus Paclitaxel (4 VS 6 Cycles) as Adjuvant Therapy for Women with 0-3 Positive Axillary Lymph Nodes: A 2X2 Factorial Phase III Randomized Study			
<b>Principal Investigator:</b> LTC David E. McCune, MC			
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; LTC Tommy A. Brown, MC; MAJ Richard D. Reed, MC			
<b>Start - Completion:</b> 14 Nov 2002 - Oct 2005	<b>Funding:</b> SWOG via Henry M. Jackson Foundation		<b>Periodic Review:</b> 23 Oct 2007
<b>Study Objective:</b> Primary Objectives: (1) To determine the equivalence of paclitaxel given every two weeks with CA given every two weeks as adjuvant therapy for women with 0-3 positive axillary lymph nodes, for disease free survival. (2) To determine if longer therapy, 12 weeks, is superior to shorter therapy, 8 weeks, of either CA or paclitaxel for disease-free survival for women with primary breast cancer with 0-3 positive axillary lymph nodes.  Secondary Objectives: (1) To determine the equivalence of paclitaxel given every two weeks with CA given every two weeks, and the potential superiority of longer vs. shorter therapy, in relation to overall survival, local control (regardless of metastatic status) and time to distant metastases (regardless of local recurrence status) (2) Compare toxicities of short and long course CA and paclitaxel as adjuvant therapy for women with 0-3 positive axillary lymph node breast cancer (3) To determine the effect of long and short course CA and paclitaxel on the induction of menopause for pre-menopausal patients. (4) To assess the discrepancy of myelosuppression among the common MDR1 haplotypes in the CA treatment arm. (5) To assess the effect of MDR1 haplotypes on DFS adjusted for treatment. (6) Exploratory analysis of the effect of CYP3A5, CYP2Cs and CYP2B6 polymorphisms on DFS and toxicity.			
<b>Technical Approach:</b> This is a randomized study and patients will be stratified according to menopausal status (premenopausal vs postmenopausal) and estrogen receptor (ER)/progesterone receptor (PR) status (ER and/or PR positive or unknown vs ER and PR negative). Patients are randomized to 1 of 4 treatment arms. Arm I: Patients receive doxorubicin IV over 10-15 minutes and cyclophosphamide IV on day 1. Treatment repeats every 21 days for 4 courses. Arm II: Patients receive doxorubicin and cyclophosphamide as in arm I. Treatment repeats every 21 days for 6 courses. Arm III: Patients receive paclitaxel IV over 1 hour once weekly for 12 weeks. Arm IV: Patients receive paclitaxel as in arm III for 18 weeks. Treatment in all arms continues in the absence of disease progression or unacceptable toxicity. Lumpectomy patients must then undergo radiotherapy. Mastectomy patients undergo radiotherapy at the discretion of the treating physician. Patients are followed every 6 months for 2 years and then annually for 15 years.			
<b>Progress:</b> This protocol remained open to enrollment with six subjects enrolled, none during FY07. All six subjects continued to be followed. Update #7 and the addition of an associate investigator were submitted and approved. No adverse events were reported.			

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204008	<b>Status:</b> Ongoing
<b>Title:</b> Phase II Trial of ONTAK® in Refractory or Relapsed Advanced Non-small Cell Lung Cancer (NSCLC)		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC		
<b>Start - Completion:</b> 8 Jan 2004 - Nov 2005	<b>Funding:</b> Ligand Pharmaceuticals, Inc. via Henry M. Jackson Foundation	<b>Periodic Review:</b> 4 Oct 2007

**Study Objective:** (1) To evaluate the safety of ONTAK® (denileukin diftitox, DAB389IL-2) in patients with NSCLC, (2) To evaluate the efficacy of ONTAK® in patients with NSCLC. (3) To evaluate the value of soluble Interleukin-2 receptors (IL2R) in predicting tumor response (or reaction) to ONTAK®. (4) To evaluate the correlation between tumor IL2R status and disease response to treatment.

**Technical Approach:** This is a Phase II multicenter non-randomized open label clinical trial. Up to 50 subjects will be enrolled in the overall study with a goal of having 42 evaluable subjects. At MAMC, 2-4 subjects may be enrolled from subjects receiving treatment for lung cancer in the Hematology and Oncology Clinic. Treatment will consist of IV administration of ONTAK® daily for 5 days every 3 weeks. Safety assessments will include laboratory hematology and blood chemistry tests, physical exam and vital signs, and ECOG status and toxicity assessments.

During the first cycle of treatment, toxicities will be evaluated weekly using the NCI Common Toxicity Criteria, then each cycle afterwards. Serious Adverse Events will be reported to the IRB, FDA, and to the study drug manufacturer. Tumor response will be assessed by physical exam, CT scan, and other appropriate imaging studies performed every 2 cycles and evaluated using the RECIST criteria. Subjects with tumor response or stable disease will receive up to 6 cycles of study treatment. Subjects with progressive disease or unacceptable toxicity will be removed from the study. Interim evaluation is planned after the first 14 evaluable subjects. If no subjects experience an objective response or stable disease, then the study will be terminated. Soluble IL2 receptor (IL2R) levels in serum will be measured to study the value in predicting tumor reaction or response to the treatment, and evaluation of tumor IL2R status and CD 25 staining will be performed by the central study site laboratory. Primary efficacy endpoints are the response rate, overall survival, and time to disease progression. Primary safety endpoints are the number of cycles of therapy administered and the type and grade of toxicities. Secondary endpoints will be the level of soluble IL-2 receptor in serum and receptor expression in the tumor tissue (positive or negative).

**Progress:** This protocol closed enrollment in January 2005, with two subjects consented and enrolled. Both subjects are now deceased and the study remained ongoing during FY07 to complete a formal site close-out by the study sponsor (date not yet set at the time of this report).

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204035	<b>Status:</b> Ongoing
<b>Title:</b> CTSU NCIC CTG MA.27, A Randomized Phase III Trial of Exemestane Versus Anastrozole in Postmenopausal Women With Receptor Positive Primary Breast Cancer		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 12 May 2004 - Jan 2010	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 22 Jan 2008

**Study Objective:** Primary objective: Compare event free survival (EFS) between women treated with exemestane or Anastrozole as adjuvant therapy. Secondary objectives are to compare: (1) overall survival(OS) of women treated with exemestane with that of those receiving Anastrozole as adjuvant therapy, (2) the time to distant recurrence for women treated with exemestane with that for women receiving Anastrozole as adjuvant therapy, (3) the incidence of new primary contralateral breast cancer in the different treatment groups, (4) the incidence of all clinical fractures and specifically hip and vertebral fractures in the different treatment groups, and (5) cardiovascular morbidity and mortality (i.e. significant coronary heart disease, which includes myocardial infarctions and angina requiring percutaneous transluminal coronary angioplasty or coronary artery bypass graft, fatal and nonfatal strokes and all vascular deaths) between exemestane and Anastrozole.

Note: Study objectives looking at the use of Celecoxib in this patient population were discontinued, 17 Dec. 04.

**Technical Approach:** This study compares two different aromatase inhibitors in an attempt to establish standard of care for this type of breast cancer. Eligible subjects will be randomized to receive either Exemestane or Anastrozole. Treatment period will be 5 years except in cases of unacceptable side effects or disease recurrence.

Note: The randomization in a double-blinded fashion to receive either Celecoxib or placebo was discontinued Dec 04, due to increased frequency of fatal and non-fatal cardiovascular events observed on the celecoxib arm of an NCI sponsored study of the prevention of colorectal polyps.

**Progress:** This protocol was reported closed to enrollment during FY06, except for some sites that are performing specific sub-studies. Ten subjects enrolled at MAMC and remain in treatment or follow-up. Multiple external adverse events were reported. Amendment #5, #6 and #7 changes to the protocol were submitted and appropriately approved as required during FY07 (MAMC is not a participant in the ongoing sub-studies).

### Detail Summary Sheet

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<b>Date:</b> 30 Sep 07	<b>Number:</b> 204043	<b>Status:</b> Ongoing
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**Title:** CTSU IBCSG Trial 25-02, Tamoxifen and Exemestane Trial (TEXT), A Phase III Trial Evaluating the Role of Exemestane Plus GnRH Analogue as Adjuvant Therapy for Premenopausal Women with Endocrine Responsive Breast Cancer

**Principal Investigator:** LTC David E. McCune, MC

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<b>Department:</b> Medicine/Hematology & Oncology	<b>Facility:</b> MAMC
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**Associate Investigator(s):** MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC; LTC Tommy A. Brown, MC; LTC Jane Shen-Gunther, MC; MAJ Richard D. Reed, MC

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<b>Start - Completion:</b> 12 May 2004 - Feb 2009	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 22 Jan 2008
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**Study Objective:** Evaluate the worth of ovarian function suppression (achieved by long-term use of GnRH analogue) plus exemestane compared with GnRH analogue plus Tamoxifen for premenopausal women with steroid hormone receptor-positive early invasive breast cancer.

**Technical Approach:** This trial compares two different types of hormonal therapy for the prevention of relapse after breast cancer surgery. Subjects may either receive no chemotherapy or commence chemotherapy at the same time that GnRH analogue is initiated. Eligible subjects will be randomized into one of two groups; surgery plus GnRH analogue and tamoxifen for 5 years or surgery plus GnRH analogue plus exemestane for 5 years.

**Progress:** This protocol remains open to enrollment, with one subject enrolled, but transferred to Swedish Hospital and Medical Center, Seattle, WA. Amendment #2 changes to the protocol, safety updates to the consent form, and the addition of an associate investigator were submitted and approved during FY07. Multiple external adverse events were reported.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 204044		<b>Status:</b> Ongoing	
<b>Title:</b> A Phase III Study of Delayed vs. Immediate Second-line Therapy with Docetaxel after Gemcitabine + Carboplatin in Advanced Non-Small Cell Lung Cancer, Protocol Number B9E-US-S245					
<b>Principal Investigator:</b> LTC David E. McCune, MC					
<b>Department:</b> Medicine/Hematology & Oncology				<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC					
<b>Start - Completion:</b> 1 Apr 2004 - Apr 2007		<b>Funding:</b> Eli Lilly via Henry M. Jackson Foundation		<b>Periodic Review:</b> 27 Feb 2007	
<b>Study Objective:</b> Primary Objective is to test the value in terms of overall survival of immediate sequential therapy with docetaxel compared to traditional second-line therapy with docetaxel at the time of progression after standard Carboplatin and Gemcitabine in patients with stage IIIb and IV non-small cell lung cancer. Secondary Objectives: (1) to assess the response rate and time to disease progression, (2) to compare toxicity in these two groups and (3) to compare quality of life using the LCSS patient scale.					
<b>Technical Approach:</b> This is a multicenter open-label randomized phase III trial to evaluate the respective response rates, time to disease progression, survival time, toxicity, and quality of life of immediate sequential therapy with docetaxel compared to traditional second-line therapy with docetaxel at the time of disease progression, after standard Carboplatin and gemcitabine in subjects with stage IIIb and IV non-small cell lung cancer (NSCLC). Up to 5 MAMC subjects may participate, with 550 subjects in the overall study. Duration of individual participation will be up to 36 months. The study will enroll chemotherapy-naïve subjects whose NSCLC is advanced at diagnosis or has recurred or progressed following surgical treatment and/or radiation therapy, and who meet additional eligibility criteria.					
Following screening, eligible subjects will receive the first phase of treatment with gemcitabine and Carboplatin chemotherapy on Day 1 and Day 8 every 21 days, followed by one week of rest, for four cycles. Safety and response will be monitored. Disease restaging will be done at the end of first phase treatment. Subjects with complete or partial response or stable disease after initial therapy will be rescreened and eligible subjects will be randomized (1:1) to the second phase treatment with immediate or delayed docetaxel. Subjects found to have progressive disease after initial therapy or who discontinue prior to completion of 4 cycles will be followed for survival data. Subjects randomized to delayed therapy will be monitored every three weeks prior to treatment. Radiological imaging of tumor sites will be performed every 3 months or as clinically indicated. With evidence of disease progression, subjects begin treatment with docetaxel. Subjects randomized to receive immediate sequential docetaxel and subjects initiating traditional treatment after progression will receive docetaxel on Day 1 every 3 weeks for a maximum of 6 cycles. Response and safety will be monitored. Subjects who complete the protocol or who discontinue study chemotherapy early will be followed at protocol intervals until progression or death. The primary endpoint is survival and will be measured from time of randomization to date of death for all randomized subjects. Secondary endpoints of response rates, time to progression, toxicity, and LCSS will be compared between regimens. An independent Data Safety Monitoring Board will assess safety at the time of formal interim analysis, planned when 50% of subjects in each docetaxel treatment arm have 1) died, 2) are lost to follow up prior to 24 months, or 3) have been followed up for at least 24 months.					
<b>Progress:</b> This protocol closed enrollment in October 2005, with seven subjects consented. Five subjects are deceased due to non-study related deaths and two subjects continued to be followed. No adverse events were reported during FY07; no changes to the protocol have been submitted.					

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204073	<b>Status:</b> Completed
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**Title:** A Multicenter, Randomized, Phase III Study of Rituximab versus Iodine I 131 Tositumomab Therapeutic Regimen for Patients with Relapsed Follicular Non-Hodgkin's Lymphoma, Protocol CCBX001-049

**Principal Investigator:** LTC David E. McCune, MC

<b>Department:</b> Medicine/Hematology & Oncology	<b>Facility:</b> MAMC
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**Associate Investigator(s):** MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; LTC Maricela Contreras, MC; COL Marc G. Cote, MC; LTC Antonio G. Balingit, MC; Jane E. Besich-Carter, BS, BCNP

<b>Start - Completion:</b> 26 Jul 2004 - Jun 2016	<b>Funding:</b> Corixa Corporation via Henry M. Jackson Foundation	<b>Periodic Review:</b> 20 Apr 2006
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**Study Objective:** (1) To compare the event-free survival, as assessed by a Masked Independent Randomized Radiographic and Oncologic Review (MIRROR) Panel, of patients treated with rituximab to that of patients treated with the Iodine I-131 Tositumomab therapeutic regimen in patients who have had at least one, but no more than two, prior therapies for follicular non-Hodgkin's lymphoma (NHL). (2) To compare confirmed response rates, durations of response, time to next treatment, and progression-free survival of patients treated with rituximab to that of patients treated with the Iodine I-131 Tositumomab therapeutic regimen in patients who have had at least one, but no more than two, prior therapies for follicular NHL, as assessed by a MIRROR panel, to compare overall survival in these two treatment groups, and to assess and compare the safety of rituximab and Iodine I-131 Tositumomab when administered to this patient population. (3) To summarize safety and efficacy outcomes during follow-up after subsequent therapy for NHL for patients in both arms who receive additional therapy.

**Technical Approach:** This is a multicenter, randomized, Phase 3 trial to compare rituximab and the Iodine I 131 Tositumomab therapeutic regimen in the treatment of subjects with follicular non-Hodgkin's B-cell lymphoma. Randomization will be stratified by prior rituximab treatment, first versus second relapse, and region, (US or outside the US). In Arm A, subjects will receive 375 mg/m<sup>2</sup> of rituximab as an IV infusion once weekly for 4 weeks. In Arm B, subjects will undergo a two phase treatment. In the dosimetric phase, subjects will receive an infusion of unlabeled Tositumomab (450mg) immediately followed by an infusion of 5 mCi (0.18 GBq) of Iodine I 131 Tositumomab (35 mg.) Whole body gamma camera scans will be obtained 3 times after the dosimetric dose. A patient-specific administered activity of Iodine I 131 Tositumomab will be calculated to deliver the desired total body dose of radiation (65 or 75 cGy).

In the second phase (therapeutic dose), subjects in Arm B will receive an infusion of unlabeled Tositumomab (450mg) immediately followed by infusion of the patient-specific activity of Iodine I 131-conjugated Tositumomab (35 mg.) Thyroid blockade will be implemented 24 hours prior to the dosimetric dose and continued for 14 days following. Hematology and serum chemistry will be measured for safety assessments weekly (hematology) and approximately monthly (chemistry) through Week 13, then at scheduled study follow up visits. Approximately 506 subjects will be randomized in the trial, and about 6 will participate at MAMC. The study will be conducted in the Hematology and Oncology Clinic in collaboration with the Nuclear Medicine Service. Subject accrual will continue for about 2 years. Subjects will be followed for response and safety measurements at weeks 7 and 13 and every 3 months for the first and second year, every 6 months for the third year, annually for the fourth and fifth years, then for long term follow up for survival, safety, and additional therapy data through year ten. After subsequent NHL therapy, follow up will assess tolerance of next anti-lymphoma therapy, development of NDS/AML, HAMA, or hypothyroidism, unexpected safety issues, and death.

The primary analysis is the intent to treat comparison of event-free survival between treatment arms, which will be based on the MIRROR panel assessment of event-free survival. Secondary analyses will include the comparison of response rates and complete response rates (confirmed) and separate analyses will evaluate other responses, duration, time to next treatment, and overall survival. Secondary and exploratory analyses will include a stratified log rank test adjusting for stratification. Kaplan-Meier formula will be used to estimate duration curves and percentiles. Estimates and confidence limits will be calculated by the product limit method and Greenwood's formula for variance. Safety will be summarized within treatment arms and compared across treatment arms.

**Progress:** This protocol was reported as completed in June 2007, with no subjects screened or enrolled. No activity occurred on this protocol during FY07.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204080	<b>Status:</b> Ongoing
<b>Title:</b> Protocol U2963n: The National Lymphocare Study: An Observational Study of Treatment, Outcomes, and Prognosis in Patients With Follicular Non-Hodgkin's Lymphoma		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC		
<b>Start - Completion:</b> 16 Aug 2004 - Aug 2014	<b>Funding:</b> Genentech via Henry M. Jackson Foundation	<b>Periodic Review:</b> 24 Apr 2007

**Study Objective:** The objective of this study is to delineate differences in treatment outcome for patients with follicular non-Hodgkin's lymphoma (NHL) by comparing the outcomes and safety of common front-line and subsequent therapeutic strategies. The planned comparisons address clinical questions including the role of watchful waiting, use of anthracyclines in front-line therapy, and role of maintenance therapy, and treatment sequencing. Reported outcomes for a given treatment strategy will include a description of these outcomes based on Follicular Lymphoma International Prognostic Index (FLIPI) score risk stratification at the time of diagnosis and subsequent treatment initiation.

**Technical Approach:** This is a prospective, observational, longitudinal, multicenter study of patients with newly diagnosed follicular Non-Hodgkin's Lymphoma (NHL). 12-18 patients may be enrolled at MAMC, and approximately 5000 patients in the United States. A database will be created containing patient and tumor characteristics and treatment and outcome information. All patients at participating sites diagnosed with follicular NHL within 6 months prior to enrollment will be eligible, regardless of specific treatments received (including investigational products) and including patients followed using a watch-and-wait approach. Patients will receive treatment and evaluations for NHL according to the treating physician's standard of care and clinical practice. No study-specific visits, interventions or patient evaluations will be conducted. Patient data will be collected from medical records and reported by means of a Web-based Electronic Data Collection System (EDC). All treatments patients receive for NHL will be recorded and treatment outcomes will be collected quarterly. Enrolled patients will be followed for up to 10 years or until death, withdrawal of consent, loss to follow up, or study termination. Study feasibility reviews will be conducted at 2, 5, 7, and 10 years. Outcome measures include: time from initial diagnosis to initial therapy; time from initial therapy to subsequent therapy, response to treatment (initial and subsequent) as assessed by the treating physician; time to disease progression; survival time; lymphoma treatment-related toxicity as measured by death, early treatment discontinuation, and hospitalization; and FLIPI score. This is an observational cohort study and is not designed to evaluate a predefined hypothesis. However, effectiveness and safety outcomes will be analyzed, confidence intervals for differences will be reported, and standard statistical tests will be performed, with the first evaluation taking place after approximately 500 patients have been enrolled for at least 6 months.

**Progress:** This observational protocol closed enrollment in February 2007, with six subjects were consented, two during FY07. One subject died and the other five remain in follow-up.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204107	<b>Status:</b> Ongoing
<b>Title:</b> CTSU ACOSOG-Z9001, A Phase III Randomized Double-blind Study of Adjuvant STI571 (Gleevec™) Versus Placebo in Patients Following the Resection of Primary Gastrointestinal Stromal Tumor (GIST)		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 1 Nov 2004 - Aug 2008	<b>Funding:</b> ACOSOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 24 Jul 2007

**Study Objective:** Primary Objective: To ascertain whether patients with resected primary GIST who are randomized to the STI571 Arm have longer recurrence-free survival as compared to the patients randomized to the Placebo Arm. Secondary Objectives: (1) To ascertain whether patients with resected primary GIST who are randomized to the STI571 Arm have longer survival as compared to the patients randomized to the Placebo Arm. (2) To obtain from patients with GIST: tumor tissue (before therapy with STI571 and if the patient develops recurrence), blood specimens (before therapy with STI571), and serum specimens (before therapy with STI571, after completing therapy with STI571, and if the patient develops recurrence) for scientific correlative analyses. (3) To assess the safety/efficacy of oral STI571 therapy in the adjuvant setting.

**Technical Approach:** Patients will be randomized into one of two groups; four 100mg capsules for a total of 400mg of the experimental drug or placebo by mouth every day for 1 year. Weight should be measured at home two times per week and the physician called if there is a weight change by more than 4 pounds from the weight taken at the last clinic visit. Patients will have a physical exam before the start of drug or placebo and then seen in the clinic weekly the first 2 weeks, at weeks 4, 6 and 8, at 3, 4, 5 and 6 months, every 3 months until year 2, every 6 months until year 5 and then every year until death.

Tumor tissue will be sent to a central pathologist to confirm the diagnosis of GIST and if it has a protein called Kit, as the presence of this protein is required for the Gleevec to work. If the tissue sample results show that the tumor is not GIST or if the Kit protein is not there, the study drug will be stopped and patients will have a physical examination and a blood test about 30 days after the study drug is stopped. These patients will continue to be contacted by phone every 3 months for 1 year, every 6 months for 3 years, and then every year until death.

**Progress:** The study sponsor closed enrollment in this protocol in April 2007, when an interim analysis confirmed that Gleevec was beneficial to patients with GIST. One MAMC subject enrolled was found to be taking placebo and has since begun open-label treatment with Gleevec. The study remains ongoing to continue study treatment for this subject. Multiple external adverse events have been reported. Amendment #6R1 and #7 changes to the protocol, and safety updates to the consent form were also submitted and approved.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204114	<b>Status:</b> Ongoing
<b>Title:</b> A Phase II Trial of Weekly Docetaxel plus Every 3-Week Carboplatin in Patients with Stage IIIB/IV Non-small Cell Lung Cancer, Protocol GIA 12156		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC		
<b>Start - Completion:</b> 27 Oct 2004 - Nov 2007	<b>Funding:</b> Aventis Pharmaceuticals, Inc. via Henry M. Jackson Foundation	<b>Periodic Review:</b> 24 Jul 2007

**Study Objective:** Primary Objective is to determine overall response rate for patients with advanced non-small cell lung cancer treated with weekly docetaxel 35 mg/m<sup>2</sup> on days 1 and 8 plus carboplatin (AUC 6) on day 1 every 21 days. Secondary Objectives are to determine the 1-year survival rate, the median overall survival rate, and to evaluate the safety and toxicity associated with this regimen.

**Technical Approach:** This trial is a two-stage, phase II study of weekly docetaxel 35 mg/m<sup>2</sup> infused on days 1 and 8 plus carboplatin (AUC 6) on day 1 only, repeated every 21 days (cycle) in patients with stage IIIB or IV advanced non small cell lung cancer who have not received prior chemotherapy. 4-6 MAMC subjects are expected to be enrolled. A total of 29 patients may be enrolled in the study overall. Physical examination and history, baseline tumor assessments, ECOG performance status, CBC, serum chemistry, EKG, and serum HCG as appropriate, will be evaluated prior to study treatment. A minimum of two courses of treatment will be given unless there is progression of disease or significant adverse reactions occur. Patients will be monitored after every two cycles (6 weeks) for tumor response using standard radiographic imaging. Objective response will be evaluated using the RECIST criteria (Response Evaluation Criteria In Solid Tumors). Clinical and laboratory toxicities will be assessed and graded according to the NCI Common Toxicity Criteria, version 2.0. Appropriate supportive care treatment will be administered. Chemotherapy dose adjustments will be made based on the organ system exhibiting the greatest degree of toxicity. Eligible patients will be treated for 2 additional cycles after best documented tumor response. All patients will be followed after treatment at defined intervals for survival data.

The primary endpoint of this study is overall response rate (complete response plus partial response). Ten patients will be enrolled into the first stage. If at least 1 patient responds, 19 additional patients will be enrolled into the second stage of the study. If at least 5 of 29 evaluable patients exhibit an objective response at the end of the second stage, the conclusion will be that this regimen is worthy of further study. Secondary endpoints will be reported for the 1-year survival rate, the median overall survival rate, evaluations of safety and toxicity associated with this regimen. The primary efficacy analysis will be conducted on all patients who receive the study drug. Objective tumor response rate along with exact 95% binomial confidence intervals will be calculated. Time-to-event outcomes including 1-year survival, time to disease progression, and duration of response will be estimated using the Kaplan- Meier product limit method. Median and quartile estimates for each time-to-event outcome will be obtained from the Kaplan-Meier estimates.

**Progress:** This protocol closed enrollment with only one subject enrolled who remains in follow-up for survival information. No changes to the protocol or adverse events have been reported.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205070	<b>Status:</b> Terminated
<b>Title:</b> A Phase II Study Using Alemtuzumab Combined with Fludarabine for the Treatment of Relapsed/Refractory B-cell Chronic Lymphocytic Leukemia (B-CLL)		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC		
<b>Start - Completion:</b> 13 Jul 2005 - Jun 2010	<b>Funding:</b> Berlex Laboratories via Henry M. Jackson Foundation	<b>Periodic Review:</b> 20 Apr 2006

**Study Objective:** The primary objective is to evaluate complete response rate in patients receiving combination treatment with Alemtuzumab and fludarabine. The secondary objectives are to evaluate over all response rate, survival at 1 year, time to progression, duration of response, adverse event profile, minimal residual disease and lymphocyte and lymphocyte subset recovery.

**Technical Approach:** This is a Phase II, open label trial of the combination of alemtuzumab and fludarabine for the treatment of relapsed/refractory B-cell chronic lymphocytic leukemia. This study will evaluate the response rate, survival, time to progression, duration of response lymphocyte subset recovery and safety profile of the combination of subcutaneous alemtuzumab and fludarabine. Patients will receive four 28-day cycles of treatment with alemtuzumab 30 mg subcutaneously followed by 25mg/m<sup>2</sup> IV of fludarabine, daily on days 1 through 5. At the end of 4 cycles, patients will have an interim assessment to determine response to treatment. This will include radiographs as needed and a bone marrow biopsy. Minimal residual disease assessment will be performed on the marrow samples. Patients who have respond or have stable disease will receive two additional cycles of chemo as in Cycles 1-4. After treatment is completed, subjects will be followed up every 6 months for disease assessment, CMV, and flow cytometry for lymphocyte subset analysis to be done monthly until CD4 and CD8 T cell counts recover to >200 cells/uL.

All patients will be prescribed Bactrim for PCP prophylaxis and famcyclovir for HSV prophylaxis starting with Day 1, and continuing for at least 2 months after treatment, or until CD4 counts are >200 cells/ uL. Patients will be monitored for CMV status throughout the study and for 6 months after treatment. If patients become CMV positive they will receive appropriate anti-CMV therapy and may have study drug delayed until CMV treatment is complete. Growth factors may be used at the discretion of the investigator for Grade 3 or 4 neutropenia, however TPO and pegfilgrastim will not be allowed. Toxicities will be graded at each study visit according to the National Cancer Institute (NCI) Common Toxicity Criteria (CTC) Version 3.0 Safety will be assessed through physical examinations and laboratory assessments at each study visit.

**Progress:** This protocol closed to enrollment in September 2006. The Sponsor completed a site close-out visit in October 2006. No subjects were screened or enrolled.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205087	<b>Status:</b> Ongoing
<b>Title:</b> A Phase II, Open Label, Multi-center Study of EP2101 Therapeutic Vaccine in Patients with Stage IIIB, Stage IV, or Recurrent Non-Small Cell Lung Cancer (NSCLC)		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC; LTC Mark L. Nelson, MC		
<b>Start - Completion:</b> 21 Sep 2005 - Jul 2010	<b>Funding:</b> Epimmune via Henry M. Jackson Foundation	<b>Periodic Review:</b> 13 Nov 2007

**Study Objective:** (1) To compare the overall survival of patients with stage IIIB, IV, or recurrent non-small cell lung cancer treated with EP2101 therapeutic vaccine to a concurrent non-HLA-A2 observation group and historical controls. (2) To evaluate the safety of EP2101 therapeutic vaccine. Secondary: (1) To determine progression-free survival time in patients treated with EP2101 therapeutic vaccine. (2) To determine the frequency, magnitude, and breadth of cytotoxic and helper T-Cell responses to EP2101 vaccine epitopes.

**Technical Approach:** At MAMC, the study will be conducted by the Hematology/Oncology Service with up to 12 MAMC subjects expected to enroll, about 6 in the vaccine group and 6 in the observational group. A total of 168 subjects may be enrolled in the study overall. Patients who qualify will be consented to have their HLA type tested. Patients who do not qualify for the vaccine portion of the trial will be consented for the observational arm if they are interested. They will have a baseline medical history and physical, QOL, laboratory testing including CBC, chemistry, urinalysis and pregnancy test if applicable. Observational patients will be seen at Wk9, Wk18, Wk22, Mo6, Mo7, Mo9, Mo12, then every three months for years 2 and 3, and annually for years 4 and 5. Visits will include QOL, con meds, disease progression and survival status.

Patients who qualify for the vaccine arm of the trial (HLA type A2) will be consented and have the following pre-study assessment: complete medical history and physical exam, ECOG status performance, concomitant medications, laboratory testing including CBC, chemistry, ANA (autoimmunity), urinalysis and pregnancy testing if applicable, ophthalmic exam, disease assessment by CT or MRI scan, and Quality of Life (QOL) questionnaire. These patients will also be referred out to another facility to have leukapheresis performed, or have a 215 ml blood sample collected using a pediatric blood unit collection bag, to submit for immunogenicity and helper T-cell assays. Patients will receive the study vaccine once every three weeks for 6 cycles, for a total of 18 weeks of treatment. Patients will be monitored by the research nurse in the clinic for observation for 60 minutes after each vaccine, to assess for adverse events. At Wk 9 and 18, patients will have disease assessments done by CT or MRI, QOL, and laboratory tests including urinalysis, ANA, and blood collected for immunogenicity and helper T-cell assays. After treatment, patients will be followed at WK 22 and Mo7 for physical exam and ECOG score, laboratory tests including CBC and chemistry, adverse event and con med assessment and survival status. In addition, at Mo6, Mo 9 and Mo12, assessments will include disease progression monitored with CT or MRI, QOL, and laboratory tests including urinalysis, ANA, and blood collected for immunogenicity and helper T-cell assays. Long term follow up assessment of survival status will be scheduled every three months for years 2 and 3, then annually for years 4 and 5.

Toxicities will be graded at each study visit according to the National Cancer Institute (NCI) Common Toxicity Criteria (CTC) Version 3.0. Patients will be withdrawn from treatment for > Grade 2 toxicity of allergic reaction, hypersensitivity, autoimmune reaction or vasculitis, or for > Grade 3 cytokine-like release reaction or local skin reaction. The study will be placed on hold for safety review if toxicities exceed the safety criteria outlined on Pg 37 of the protocol.

**Progress:** This protocol closed enrollment in February 2006, as the addition of ongoing booster shots for enrolled subjects limited the supply of available vaccine. The protocol remains ongoing with four subjects screened and three enrolled. One subject progressed and was withdrawn, and the other two subjects remain in follow-up. Two external serious adverse events were reviewed and submitted to the IRB. There have been no changes reported to the protocol.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205093	<b>Status:</b> Completed
<b>Title:</b> A Phase 3, Double-Blind, Placebo-Controlled Study of Maintenance Premetrexed plus Best Supportive Care versus Best Supportive Care Immediately Following Induction Treatment for Advanced Non-Small Cell Lung Cancer AND COMPANION STUDY Companion Translational Research Protocol		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC		
<b>Start - Completion:</b> 27 Oct 2005 - Aug 2010	<b>Funding:</b> Eli Lilly and Company via Henry M. Jackson Foundation	<b>Periodic Review:</b> 20 Jul 2006

**Study Objective:** (1) To compare maintenance therapy with Premetrexed plus best supportive care (BSC) versus placebo plus BSC, in terms of the overall survival time (OS) in patients with Stage IIIB (with pleural effusion and/or positive supraclavicular lymph nodes) or IV NSCLC who have not progressed during four cycles of platinum-based induction chemotherapy. (2) To compare the following between the randomized treatment arms: Time to event efficacy endpoints: Progression-free survival time (PFS), Time to objective progressive disease (TPD), Time to worsening of symptoms (TWS), Objective tumor response rate, Adverse events, and Changes in individual symptom scores and quality of life using the Lung Cancer Symptom Scale (LCSS).

**Technical Approach:** This is a phase 3, global, multicenter, randomized, double-blind, placebo-controlled study to compare maintenance therapy with Premetrexed plus BSC versus placebo in terms of overall survival time in patients with stage IIIB (with pleural effusion and/or positive supraclavicular lymph nodes) or stage IV NSCLC who have not progressed during four cycles of platinum-based induction chemotherapy. Eligible patients will be randomly assigned to receive Premetrexed plus BSC or placebo plus BSC. Patients in both treatment arms will receive folic acid, vitamin B12 supplements and dexamethasone. Each patient will undergo a treatment period and a follow-up period. The treatment period consists of 21 day treatment cycles. Patients will receive treatment (control or experimental) until objective disease progression. The follow-up period begins when the patient discontinues study treatment. Patients are to be followed with a periodic tumor response evaluation until objective disease progression. All patients will be followed until death or study closure.

The study will apply technology to evaluate intratumoral gene expression, followed by protein expression and DNA polymorphisms of key genes involved in the cellular transport, activation and cytotoxic activity of Premetrexed. All subjects entered into the clinical study will be invited to participate in the companion protocol. Samples will be shipped to the sponsor Eli Lilly and Company and will be stored for a maximum of 3 years after the companion study is completed and then the tissue samples will be destroyed.

**Progress:** This study was closed by the study sponsor in June 2007, due to a change in standard treatment for the subject population that affected enrollment. No subjects were screened or enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206013	<b>Status:</b> Terminated
<b>Title:</b> SWOG S0435 A Phase II Trial of BAY 43-9006 (SNC-724772) in Patients with Platinum-Treated Extensive Stage Small Cell Lung Cancer		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 18 Jan 2006 - Nov 2010	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 21 Nov 2006

**Study Objective:** Primary endpoints: to evaluate the efficacy of BAY 43-9006 in previously-treated, platinum-sensitive and platinum-refractory patients with measurable disease and extensive stage small cell lung cancer (E-SCLC) in terms of response rate (confirmed and unconfirmed, complete and partial). Secondary endpoints: to assess the qualitative and quantitative toxicities of BAY 43-9006 in this patient population. To assess overall survival in this group of patients treated with BAY 43-9006. To collect specimens via the Lung Cancer Specimen Repository Protocol (S9925) in order to perform exploratory analyses of the relationship between selected markers and patient outcomes.

**Technical Approach:** This is a Phase II, multi-center trial of BAY 43-9006 in patients with platinum-treated extensive stage small cell lung cancer. BAY-43-9006, or Sorafenib, is a compound that inhibits multiple tyrosine kinase pathways involved in tumor progression. Patients will be enrolled who have had prior treatment with platinum based therapy. Accrual will proceed separately in two strata based on whether patients are platinum sensitive or resistant. Patients will undergo screening, with medical history and physical, head and chest CT scans, bone scan if indicated, and blood tests for chemistry and CBC. Patients will also be offered participation in S9925, a companion study for specimen submission. Eligible patients will be treated with an oral dose of BAY 43-9006, 400mg twice a day in a 4 week cycle until disease progression. Ongoing assessments will include weekly toxicity assessment, CBC every other week, and physical exam chemistry every 4 weeks. Disease assessment will include scans every 8 weeks during treatment, and every 3 months after treatment for up to 2 years after enrollment, or until death. Enrollment will continue until 20 each of platinum sensitive and platinum resistant patients have been enrolled, after which an additional 20 patients will be enrolled to each group if there has been at least one response to treatment.

**Progress:** This protocol was reported as closed to enrollment 30 January 2007, once the accrual goal was met. One subject enrolled at MAMC, was removed from the study a week later due to toxicity, and died a month later due to progressive disease. The protocol was terminated at MAMC in February 2007.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206014	<b>Status:</b> Completed
<b>Title:</b> A Phase I/II Trial of Zometa in Patients with Monoclonal Gammopathy of Undetermined Significance (MGUS)		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC		
<b>Start - Completion:</b> 6 Jun 2006 - July 2010	<b>Funding:</b> Oncotherapeutics via Henry M. Jackson Foundation	<b>Periodic Review:</b> 16 Oct 2006

**Study Objective:** To determine the effect of zoledronic acid on bone mineral density (BMD) of lumbar spine, utilizing dual energy x-ray absorptiometry (DEXA) scan, among patients with MGUS with associated osteopenia/osteoporosis. The secondary objectives of this study are to: determine the effect of zoledronic acid on skeletal fractures in MGUS patients with osteopenia/osteoporosis, determine the effect of zoledronic acid on BMD of total hip, determine the effect of zoledronic acid on serum M-protein levels, determine the proportion of patients treated with zoledronic acid that develop multiple myeloma or other related malignancies, and determine the safety of the use of zoledronic acid in the treatment of MGUS patients with osteopenia/osteoporosis.

**Technical Approach:** This is an open label study designed to evaluate the efficacy and safety of zoledronic acid in MGUS patients with osteopenia/osteoporosis. A screening visit will be conducted within 14 days before baseline (baseline being prior to the administration of the first dose of study drug). At this visit, a medical history will be obtained and a complete physical examination will be performed including vital signs, weight, 12-lead electrocardiogram, and postero-anterior and lateral chest x-rays. Pre-study disease assessment will be performed, including bone mineral density (BMD) of lumbar spine, Karnofsky Performance Status (KPS), skeletal survey, bone marrow aspirate and biopsy (patients will be required to have this procedure if bone marrow aspirate and biopsy has never been performed to rule out the possibility of malignancy), serum and urine protein electrophoreses. The bone marrow aspirate and biopsy will be evaluated for degree of plasma cell involvement. Clinical laboratory tests including hematology, clinical chemistry (including electrolytes, calcium, magnesium and random glucose), liver tests, urinalysis, and serum pregnancy tests for women of child-bearing potential will also be performed at the Screening visit. Patients who meet the eligibility requirements as assessed at the Screening visit will be enrolled in the study. Zoledronic acid at 4 mg will be administered intravenously every 6 months over a period of 12 months. Patients are to attend a Final study visit. Procedures to be conducted at this visit include a complete physical examination, adverse event assessment, vital signs, Karnofsky performance status assessment and clinical chemistry.

**Progress:** The study sponsor reported this protocol closed to enrollment in February 2007. A final close out visit was conducted and the protocol reported completed at MAMC with no subjects screened or consented.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206054	<b>Status:</b> Ongoing
<b>Title:</b> NSABP B-38 A Phase III Adjuvant Trial Comparing Three Chemotherapy Regimens in Women with Node-Positive Breast Cancer: Docetaxel/Doxorubicin/Cyclophosphamide (TAC); Dose-Dense (DD) Doxorubicin/Cyclophosphamide Followed by DD Paclitaxel (DD AC-P); DD Doxorubicin/Cyclophosphamide Followed by DD Paclitaxel Plus Gemcitabine (DD AC-PG)		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC		
<b>Start - Completion:</b> 12 Apr 2006 - Feb 2011	<b>Funding:</b> SWOG?	<b>Periodic Review:</b> 2 Jan 2008

**Study Objective:** The primary aims of this study are to determine whether the DD AC/PG regimen is superior to the TAC regimen as well as to the DD AC/P regimen in improving disease-free survival and to compare the relative disease-free survival of TAC and DD AC/P. Secondary aims are to determine whether DD AC/PG is superior to TAC as well as to DD AC/P in improving overall survival, recurrence-free interval, and distant recurrence-free interval; to compare overall survival, recurrence-free interval, and distant recurrence-free interval of the TAC and DD AC/P regimens, and to compare the relative toxicities of the three regimens.

**Technical Approach:** This Phase III adjuvant therapy trial for women with node-positive breast cancer will compare three regimens of chemotherapy: (1) TAC: docetaxel, doxorubicin, and cyclophosphamide every 3 weeks for 6 cycles, (2) DD AC/P: doxorubicin/cyclophosphamide every 2 weeks for 4 cycles followed by paclitaxel every 2 weeks for 4 cycles (3) DD AC/PG: doxorubicin/cyclophosphamide every 2 weeks for 4 cycles followed by paclitaxel plus gemcitabine every 2 weeks for 4 cycles. Women with operable, invasive carcinoma of the breast with histologically positive axillary nodes will be enrolled and stratified by number of positive nodes, hormone receptor status, and type of surgery and planned radiotherapy. Following stratification, patients will be randomized to one of the three chemotherapy regimens. Women with ER positive and/or PgR-positive tumors should receive hormonal therapy for a minimum of 5 years following completion of chemotherapy. All women who have had a lumpectomy will have radiation therapy. Chest wall and regional nodal irradiation will be prospectively determined at the discretion of the investigator and will be used as a stratification factor. For patients who agree to specimen banking, index tumor blocks as well as tumor blocks collected after diagnosis of contralateral breast cancer will be submitted. Serum will be collected at baseline, at the time of first locoregional or distant recurrence, and when a contralateral breast cancer develops prior to locoregional or distant recurrence. If the first recurrence is an ipsilateral breast tumor recurrence, a serum sample will also be collected at the time of the first subsequent regional or distant recurrence. The study will enroll 4800 patients over a period of approximately 4 years. It is anticipated that the definitive analysis will be carried out approximately 7 years after study initiation.

**Progress:** This protocol closed to enrollment in April 2007, with two subjects enrolled, one during FY07. One subject completed study treatment and the other opted to discontinue treatment. Both subjects continue to be followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206055	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S0424: Molecular Epidemiology Case-Series Study of Non-Small Cell Lung Cancer in Smoking and Non-Smoking Women and Men		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 3 Aug 2006 - Feb 2011	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 22 Jan 2008

**Study Objective:** To assess lung tissue from cancer patients for specific tobacco smoke carcinogens, alterations in specific genes, and to determine whether these factors differ by gender and smoking status, adjusting for potential exposures and influential factors including family smoking status, medication use, hormonal and reproductive factors. To measure levels of (PAH)-DNA adducts in tissues and see if levels are higher in females than males for the same level of smoking.

**Technical Approach:** Eligible patients would be asked to complete a questionnaire about smoking, reproductive history, occupational exposures and other factors. Samples of cancer tissue obtained at the time of biopsy or operation would be sent to a special laboratory to study genetic changes that may explain why women are more susceptible to tobacco smoke chemicals. A blood specimen would be sent to a special laboratory for scientific testing to help learn more about the causes of lung cancer and who is at risk to identify who would benefit from intensive screening and possible interventions. The results of the testing will not be released to the patient or study physician.

**Progress:** This minimal risk epidemiology protocol remains open to enrollment, although no subjects enrolled during FY07. Revision #1, #2 and #3 and the addition of Dr. Reed as associate investigator were submitted and approved.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206073	<b>Status:</b> Terminated
<b>Title:</b> Phase 1/2 study of ZK-Epothilone (ZK-Epo; ZK 219477) in combination with carboplatin in patients with platinum-sensitive, recurrent ovarian cancer		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC		
<b>Start - Completion:</b> 11 Jul 2006 - May 2010	<b>Funding:</b> Berlex Laboratories via Henry M. Jackson Foundation	<b>Periodic Review:</b> 17 Apr 2007

**Study Objective:** Primary objective: to establish a dose of ZK-Epo to be used in combination with carboplatin in the subsequent Part 2 of the study. Secondary objective: to investigate the pharmacokinetics of ZK-Epo and carboplatin when given as a combination.

Part 2: Primary objective: to investigate the efficacy of ZK-Epo in combination with carboplatin in patients with platinum-sensitive, recurrent ovarian cancer in progression following a first regimen of chemotherapy. Secondary objective: to investigate the safety and tolerability of ZK-Epo in combination with carboplatin in this patient population.

**Technical Approach:** This is a Phase I / II, open label study of ZK-Epothilone (ZK 219477) in combination with carboplatin in patients with platinum sensitive, recurrent ovarian cancer. Patients will be eligible who have progressed after having had one prior chemotherapy regimen including a platinum compound, and who have had a response lasting between 6 and 24 months. Phase I of the study will enroll up to 18 patients in cohorts of 6. Patients will initially be treated at 12 mg/m<sup>2</sup>. Depending on the observed Dose Limiting Toxicities (DLT) the dose will either be decreased to 9 mg/m<sup>2</sup> or increased to 15 mg/m<sup>2</sup>. Patients who develop a DLT will be withdrawn from the study. Patients in Phase I will be required to participate in a pharmacokinetic study to examine the metabolism of ZK-Epo in combination with carboplatin. Patients may also participate in an optional pharmacogenetic substudy. Patients who participate in Part I who appears to benefit from treatment can continue to receive additional cycles of ZK-Epo at the dose level at which they started treatment. Phase II of the study will use the treatment dose determined in Phase I. Up to 30 patients will be enrolled, for a total of 32 evaluable patients.

Patients in both phases will be scheduled to receive 2 to 6 cycles of treatment. ZK-Epo will be given per dose escalation, as a 3-hour IV infusion, on Day 1 of a 21 day cycle. Carboplatin will be given at an AUC of 5, as a 30 minute infusion, after ZK-Epo. Patients will sign an approved consent form prior to any study-related procedures. Initial evaluation will include physical exam and history, review in inclusion criteria, disease assessment by CT, MRI or CA-125 level, EKG, and laboratory tests including CBC, chemistry and LFT's. PE and labs will be repeated for each cycles, disease assessment will be repeated every other cycle. Patients will continue treatment until they have received 6 cycles, progress, or are unable to tolerate treatment. After treatment patients will be followed until disease progression.

Pharmacokinetic studies will be done for all patients on Phase I, and is option for patients on Phase II. This will consist of thirteen 2.7ml samples drawn within the first 12 hours, and one sample on days 2, 3, 4, 5, 8 and 15. PK samples will only be drawn for the first two cycles of a patient's treatment. Additional pharmacogenetic studies are optional for all patients, and consist of a single blood sample drawn prior to initiation of therapy.

**Progress:** No subjects were screened or enrolled during FY07, resulting in termination of the protocol by the study sponsor, memo date 22 October 2007.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206084	<b>Status:</b> Terminated
<b>Title:</b> Pilot Study to Evaluate the Safety and Efficacy of PROCRIT (Epoetin alfa) 80,000 Units Once Every Four Weeks (Q4W) vs. 40,000 Units Once Every Two Weeks (Q2W) in Cancer Patients with Non-Chemotherapy Anemia		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC		
<b>Start - Completion:</b> 12 Jul 2006 - Dec 2009	<b>Funding:</b> OrthoBiotech via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** Objectives: To investigate the safety and efficacy of PROCRIT 80,000 units (U) once every 4 weeks and 40,000U once every 2 weeks subcutaneously in anemic subjects with cancer not receiving chemotherapy or radiation therapy and to assess the effects of the dosing regimens on time-to- hematopoietic-response, and transfusion requirements.

**Technical Approach:** This is a prospective, randomized, open-label, multi-center pilot study to evaluate the safety and efficacy of PROCRIT (Epoetin alfa) 80,000 Units once every four weeks versus 40,000 Units (U) once every two weeks in cancer patients with non-chemotherapy anemia. A total of 100 subjects will be enrolled and up to 10 at MAMC. Patients with confirmed non-myeloid malignancy, who are anemic, and not receiving chemotherapy or radiation will be randomized in to one of two treatment groups receiving Procrit. Safety data that will be obtained during the study includes height, weight, blood tests, blood pressure and incidence and severity of adverse events. Patients will be randomized to one of two treatments groups receiving PROCRIT subcutaneously. The starting dose will be either 80,000 U every 4 weeks with a maximum treatment period of 13 weeks or 40,000 U every 2 weeks with a maximum period of 15 weeks. A follow-up visit will occur for both treatment groups on weeks 17. Hemoglobin levels will be obtained every week to monitor hemoglobin rate of rise for safety. The target hemoglobin is 10 to 12 g/dL. Patient will be screened for study eligibility at the screening visit occurring up to 14 days prior to treatment with study drug unless otherwise specified. They will be followed up to week 17. An interim analysis will be performed when the first 40 enrolled subjects have completed or withdrew from the study. The primary efficacy end point will be hematopoietic response, defined as < 1 g/dL rise in hemoglobin.

**Progress:** This protocol was terminated at MAMC April 2007 once the study sponsor had closed enrollment. No subjects were screened, consented or enrolled. Two external serious adverse events were reviewed and submitted to DCI for the placement in the protocol file.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206112	<b>Status:</b> Ongoing
<b>Title:</b> CTSU GOG 0218, A Phase III Trial of Carboplatin and Paclitaxel Plus Placebo Versus Carboplatin and Paclitaxel Plus Concurrent Bevacizumab (NSC #704865, IND #7921) Followed By Placebo, Versus Carboplatin and Paclitaxel Plus Concurrent and Extended Bevacizumab, In Women With Newly Diagnosed, Previously Untreated, Stage III or IV Epithelial Ovarian or Primary Peritoneal Cancer		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC; LTC Louis A. Dainty, MC		
<b>Start - Completion:</b> 2 Nov 2006 - Sep 2011	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 24 Jul 2007
<p><b>Study Objective:</b> Primary objectives: Determine if the addition of 5 concurrent cycles of Bevacizumab to 6 cycles of standard treatment (carboplatin and paclitaxel) [Arm II] reduces the death rate when compared to 6 cycles of standard treatment alone [Arm I] in women with newly diagnosed suboptimal advanced epithelial ovarian and peritoneal primary cancer; determine if the addition of 5 concurrent cycles plus extended Bevacizumab for 15 months total treatment time to 6 cycles of standard therapy (carboplatin and paclitaxel) [Arm III] reduces the death rate when compared to 6 cycles of standard therapy [Arm I] in this subset of patients.</p> <p>Secondary objectives: Determine, in the event that both Arm II and Arm III regimens are superior to the Arm I regimen with respect to overall survival, whether the Arm III regimen reduces the death rate when compared to the Arm II regimen; determine whether the Arm II or Arm III regimen increases the duration of progression-free survival when compared with the Arm I regimen; compare each of the experimental regimens to the Arm I regimen with respect to the incidence of severe side effects or serious adverse events; determine the impact on quality of life following treatment with the above regimens; assess the relationship between angiogenic markers and clinical outcome (tumor response, progression-free survival, overall survival) in each of the Arms; assess the predictive value of a set of genes whose expression correlates with survival in these patients.</p> <p><b>Technical Approach:</b> This is a Phase III study of standard chemotherapy (carboplatin plus paclitaxel) versus standard plus concurrent bevacizumab versus standard plus extended bevacizumab in women with first line, advanced stage epithelial ovarian and primary peritoneal cancer. Patients with a histological diagnosis of FIGO Stage III or IV epithelial or peritoneal primary cancer, with suboptimal residual disease following initial surgery will be screened for enrollment. Patients who qualify will be enrolled and randomized in a 1:1:1 ratio to Arm I, II or III. Randomization will be stratified by stage of disease (Stages III versus IV) and by performance status (0 versus 1 or 2). All patients will receive standard chemotherapy, paclitaxel 175 mg/m<sup>2</sup> IV over 3 hours followed by carboplatin AUC 6 IV over 30 minutes on Day 1 of a 21 day cycle, over 6 cycles. Dose adjustments will be made per protocol for changes in creatinine clearance and for toxicities. Patients in Arm I will also receive placebo on Day1 of Cycle 2 through 6, the placebo every 21 days for an additional 15 months. Patients on Arm II will receive bevacizumab on Day 1 of Cycle 2 through 6, and placebo every 21 days for an additional 15 months. Patients on Arm III will receive bevacizumab on Day 1 of Cycle 2 through 6, and bevacizumab every 21 days for an additional 15 months. Bevacizumab will be given, 15 mg/mg, IV, per package insert. During initial chemotherapy, patients will be assessed at the start of each cycle by physical exam, laboratory tests including CBC, chemistry, LFTs, and CA-125. Patients on anticoagulant therapy will have a repeat PT, PTT and INR prior to each cycle. Blood pressure will be monitored at least weekly during the first cycle, then prior to each cycle afterwards. Radiographic measurements will be</p>		

repeated prior to every other cycle. During bevacizumab/placebo treatment these same assessments will be done every other cycle. Post treatment, patients will be followed every 3 months for 2 years, every 6 months for three years, then annually.

**Progress:** This greater than minimal risk protocol received initial IRB approval on 25 July 2006, and final approval was received 2 November 2006. Multiple external serious adverse events reviewed by the PI were submitted to DCI for the file. Revision #1, Revision #2, and one safety update to the consent form were submitted and approved. The study remains open to enrollment with one subject enrolled during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206126	<b>Status:</b> Ongoing
<b>Title:</b> A Phase II Trial of Imatinib (Gleevec) Plus Gemcitabine In Patients With Ovarian Carcinoma Who Have Failed At Least One Prior Chemotherapy		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 22 Nov 2006 - Oct 2011	<b>Funding:</b> Novartis via Henry M. Jackson Foundation	<b>Periodic Review:</b> 25 Sep 2007

**Study Objective:** (1) To evaluate the cytostatic, anti-tumor activity of the combination of Gleevec™ (Imatinib Mesylate) and gemcitabine via progression-free survival for at least six months in subjects with recurrent or persistent epithelial ovarian or primary peritoneal carcinoma. (2) To assess the tumor response rates using modified SWOG criteria to the combination of Gleevec™ (Imatinib Mesylate) and gemcitabine in subjects with relapsed ovarian cancer who have failed at least one prior chemotherapy treatment. (3) To determine the safety and tolerability via frequency and severity of adverse effects of combination Gleevec™ and gemcitabine in this cohort of subjects as assessed by CTC. (4) To determine the distribution of the overall survival. (5) To estimate the clinical response rate (partial and complete response as defined under the modified SWOG criteria). (6) To assess the effects of prognostic variables: initial performance status, platinum sensitivity, and mucinous (or clear cell) histology on progression-free survival overall.

**Technical Approach:** This is a Phase II, single arm, open label treatment study to evaluate the tumor response rate to the combination of Gleevec and Gemcitabine for treatment of women who have failed at least one prior chemotherapy regimen containing platinum. 60 subjects are expected to enroll to achieve a goal of 56 evaluable subjects, with 20 subjects expected to enroll at MAMC. Women will be recruited during regular visits to the Oncology Clinic; those appearing eligible will be consented and screened. Those who qualify will be given a combination of oral Gleevec and IV Gemcitabine, over a 21 day cycle, for as long as they respond and are able to tolerate the combination. Subjects experiencing side effects may receive supportive care with growth factors or antiemetics as appropriate or have their dose modified per protocol. Subjects will be followed after each cycle by physical exams, laboratory assessments including CA-125 tumor marker, and by review of adverse events and cancer-related symptoms. Tumor assessments will be done every other cycle by CT or MRI. Subjects removed from treatment will be followed every three months by clinic visit or phone contact for up to five years to determine time to progression and survival rates.

**Progress:** Approved protocol documents were released to the study staff in January 2007, following CRADA/SOW approval. Three subjects have enrolled and continue to receive study treatment. Multiple external serious adverse events have been reviewed by the PI and submitted to DCI for the file, resulting in one recommended safety update to the risks of Imatinib in the consent form. One internal adverse event was reported, hospitalization for cellulitis of the left leg, which was assessed by the PI as an expected serious complication of chemotherapy that in no way suggests a problem with this protocol. The protocol remains open to enrollment.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 207023	<b>Status:</b> Terminated
<b>Title:</b> Phase 2 study of ZK-Epothilone (ZK-Epo; ZK 219477) plus prednisone as first-line chemotherapy in patients with metastatic androgen-independent prostate cancer			
<b>Principal Investigator:</b> LTC David E. McCune, MC			
<b>Department:</b> Medicine/Hematology & Oncology			<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Richard D. Reed, MC; MAJ Jasmine T. Daniels, MC			
<b>Start - Completion:</b> 7 Feb 2007 - Jan 2012	<b>Funding:</b> Berlex Pharmaceuticals via Henry M. Jackson Foundation		<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective is to investigate the efficacy of ZK-Epo plus prednisone in patients with androgen-independent prostate cancer (AIPC) who have not had previous chemotherapy.

**Technical Approach:** This is a Phase 2, open label, first-line study of ZK-Epothilone and prednisone in androgen independent prostate cancer. This study will enroll a maximum of 46 subjects, whose disease has progressed despite hormonal therapy, using a Simon's two-step design. Stage 1 will enroll 13 evaluable subjects. If the results for the first 13 subjects meet the pre-defined criterion,  $re > 3$  PSA responders, then additional patients will be enrolled in Stage 2 to meet the goal of 46 evaluable subjects. Secondary efficacy endpoints are time to progression, time to PSA progression, and duration of response. Some screening procedures may be done as part of routine care, and will not be repeated if they fall within the screening timeframe.

Screening procedures include physical exam, medical and surgical history, concomitant medications, vitals including performance status, chest X-ray, bone scan, tumor assessment by CT or MRI, neurological score, ECG and laboratory tests including chemistry, CBC, UA and PSA. Subjects meeting the inclusion criteria will receive ZK-Epothilone, 16 mg/m<sup>2</sup> as a 3 hour infusion every 21 days, and prednisone, 5 mg orally, twice a day for 21 days. Study drug dosing will be adjusted per protocol in subjects experiencing toxicities. Prednisone compliance will be documented by the patient on the prednisone diary. Subjects will return to the clinic on days 8 and 15 for adverse event assessment and CBC. Prior to the start of each cycle subjects will have a physical exam, neurological assessment, 12-lead ECG, adverse assessment, blood and urine testing, and PSA sample to be submitted to the central lab. Tumor assessment will be done after every 2 cycles by CT or MRI in subjects who had measurable disease at baseline. Subjects who tolerate study treatment and whose disease either responds or stays stable may continue on treatment beyond 6 cycles at the investigator's discretion. Subjects who withdraw from treatment will be followed monthly for 3 months, then every three months until disease progression.

**Progress:** This protocol was initially approved by the IRB, 21 November 2006, and received final approval on 7 February 2007. The study has been terminated at MAMC by the study sponsor due to no enrollment.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 207027	<b>Status:</b> Ongoing
<b>Title:</b> Prospective, Randomized, Single-Blinded, Multi-Center Phase II Trial of the HER2/neu Peptide GP2 + GM-CSF Vaccine versus GM-CSF Alone in HLA-A2+ OR the Modified HER2/neu Peptide AE37 + GM-CSF Vaccine versus GM-CSF alone in HLA-A2- Node-Positive and High-Risk Node-Negative Breast Cancer Patients to Prevent Recurrence			
<b>Principal Investigator:</b> LTC David E. McCune, MC			
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; MAJ Richard D. Reed, MC			
<b>Start - Completion:</b> 7 Mar 2007 - Jan 2012	<b>Funding:</b> Antigen Express, Inc. and USMCI via Henry M. Jackson Foundation		<b>Periodic Review:</b> 11 Dec 2007
<b>Study Objective:</b> The objectives of this study are to determine (1) if the GP2 + GM-CSF vaccine reduces the recurrence rate in HLA-A2+, Her2/neu+ node-positive or high-risk node-negative breast cancer patients randomized to receive either the vaccine versus the immunoadjuvant, GM-CSF, alone, (2) if the AE37 + GM-CSF vaccine reduces the recurrence rate in HLA-A2-, Her2/neu+ node-positive or high-risk node-negative breast cancer patients randomized to receive either the vaccine versus the immunoadjuvant, GM-CSF, alone, (3) to monitor the in vitro and in vivo immunologic responses to the vaccines and correlate these responses with the clinical outcomes, and (4) to monitor for any unexpected toxicities with the vaccines.			
<b>Technical Approach:</b> This is a randomized, single-blinded, multi-center phase II trial of two types of vaccine for HER2/neu positive, high-risk breast cancer patients (patients who are node positive or high risk node negative). Subjects will include patients from the Oncology Clinic who have been diagnosed with HER2/neu positive breast cancer and who have completed standard treatment (including surgery, chemotherapy and or radiation therapy) within 1 to 6 months. Subjects will be identified by their treating oncologist, and will be consented by the physician during a regularly scheduled clinic visit. As part of screening, subjects will have their immune response tested using a panel of recall antigens given by Mantoux intradermal technique. This will be repeated at the end of the vaccine series. Photographs will be taken of the local reaction for documentation. Subjects who qualify will be tested for HLA type, and will be randomized in a 1:1 ratio to peptide plus GM-CSF or GM-CSF alone. Subjects who are HLA type A2 positive will receive the GP2 peptide or placebo. HLA type A2 negative subjects will receive AE37 peptide or placebo. Subjects will receive vaccine or placebo as two 0.5ml intradermal injections, within two inches of each other. Doses will be given every 3 to 4 weeks for a total of 6 sets of injections. When the vaccine portion is completed subjects will be followed as per their standard of care every 3 months for the first 24 months, then every 6 months for an additional 36 months. The clinical endpoint of recurrence will be determined by the treating physician based on standard clinical, lab and radiographic surveillance. Blood will be drawn at screening and prior to each vaccination for immunologic testing. These blood samples will be sent to the CVDL at USUHS for testing. Left over blood may be stored for up to 5 years for future immunologic testing; no genetic testing will be performed.			
<b>Progress:</b> This greater than minimal risk protocol was initially approved by the IRB 12 December 2006, and final approval received 7 March 2007. One patient enrolled during FY07, and continues to receive treatment. No unreported adverse events have occurred at the time of this report, October 2007.			

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207077	<b>Status:</b> Ongoing
<b>Title:</b> CTSU CALGB 70301, Quality of Life, Employment and Informal Care Cost Analysis in Women Receiving Adjuvant Chemotherapy for Breast Cancer with 0-3 Positive Axillary Lymph Nodes Companion to CALGB 40101		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Richard D. Reed, MC; MAJ Jasmine T. Daniels, MC		
<b>Start - Completion:</b> 19 Mar 2007 - Apr 2012	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objectives are to (1) compare the individual treatment arms relative to the degree that symptoms interfere with patient functioning and to characterize and compare the relative duration that symptoms interfere with patient functioning, (2) assess the employment consequences of cancer and its treatment on the patient and extended family and to compare treatment arms relative to these consequences, and (3) determine the prevalence and severity of peripheral neuropathy in breast cancer patients treated by adjuvant chemotherapy with dose dense (every two weeks) paclitaxel for 4 and 6 cycles, from study entry to five years after the start of treatment. The secondary objectives are to (1) identify baseline characteristics that are predictive for patients being more vulnerable to experiencing side effects which significantly interfere with patient functioning, (2) identify and characterize the relative importance of the reasons that patients decide to participate in the treatment study (CALGB 40101) and how those reasons might change as a consequence of their experience with treatment, (3) compare the quality-adjusted life years between the four treatment arms, (4) measure, over the course of adjuvant therapy, the type and amount of informal care needs of the patient using a societal perspective, estimate and compare the economic consequences on employment and informal care needs, (5) determine if specific identifiable clinical adverse events (i.e., neuropathy or fatigue) are associated with greater economic consequences, (6) examine factors which are predictive of a patient being employed during and after cancer treatment, (7) compare the prevalence and severity of peripheral neuropathy in breast cancer patients treated by dose dense paclitaxel to those patients treated with dose dense CA (cyclophosphamide and doxorubicin), (8) conduct an exploratory examination of the relationship between the severity of peripheral neuropathy after paclitaxel treatment (4 and 6 cycles) and breast cancer patients function, including physical, psychological, and social functioning, and (9) validate the neurotoxicity items in the Symptoms in Relation to Patient Functioning Survey (C-1271) used in this protocol by correlating its results with the FACT-Neurotoxicity Subscale (C-669) and the EORTC QLQ-C30 and Breast Cancer module (C-259 and C-618).

**Technical Approach:** This is an NIH sponsored, longitudinal study that assesses the impact of chemotherapy-induced symptoms on the function and quality of the lives of women who are receiving adjuvant chemotherapy for breast cancer. It is a companion study to CALGB 40101 which is a randomized, phase III trial of dose-dense cyclophosphamide and doxorubicin (CA) (4 vs. 6 cycles) versus dose-dense paclitaxel (4 vs. 6 cycles) as adjuvant therapy for breast cancer for women with 0-3 positive axillary lymph nodes. Patients must be enrolled in CALGB 40101 to be qualified for this study. MAMC is anticipating up to 10 enrollees. Methods include the collection of background information, quality of life surveys, employment and informal care cost assessments, and peripheral neuropathy assessments. Data will be used by CALGB to address the primary and secondary objectives. No data analysis will occur at MAMC.

**Progress:** This protocol was approved by the Expedited Review Committee on 19 March 2007. Revision #3 with administrative/editorial changes to the protocol was submitted and approved 9 July 2007. No subjects have enrolled.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207078	<b>Status:</b> Terminated
<b>Title:</b> An Observational Study of Avastin® (Bevacizumab) in Combination with Chemotherapy for Treatment of Metastatic or Locally Advanced and Unresectable Colorectal Cancer, Locally Advanced or Metastatic Non-Small Cell Lung (Excluding Predominant Squamous Cell Histology), or Locally Recurrent or Metastatic Breast Cancer		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> Terminated before final approval	<b>Funding:</b> Genentech, Inc. via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A
<p><b>Study Objective:</b> The effectiveness objectives for this study are to (1) describe the patterns of Avastin therapy within the first-line treatment setting (treatment until first progression vs. treatment interrupted ["drug holidays"] versus treatment discontinued prior to first progression) and to examine the association between duration of Avastin therapy and first-line treatment outcome, as measured by progression free survival (PFS), (2) describe the dose of Avastin therapy within indications and to explore the association between dose and clinical benefit, as measured by PFS, (3) examine the association between Avastin therapy across lines of therapy (treatment discontinued at or before first progression vs. continuation of treatment past first progression) and overall treatment outcome, as measured by overall survival, and (4) estimate the effectiveness of Avastin in combination with various chemotherapy regimens, as measured by best response, PFS, and overall survival.</p> <p>The safety objectives for this study are to (1) describe the incidence, potential risk factors, outcomes, and management of specific adverse events associated with Avastin treatment, including the following: hypertension requiring medical management; all gastrointestinal perforations; all serious vascular events (as defined according to the Antithrombotic Trialists' Collaboration [ATC] criteria); all arterial thromboembolic (ATE) events; all venous thromboembolic (VTE) events; bleeding events (other than pulmonary hemorrhage) requiring transfusion, major/non-elective intervention, or was life-threatening; severe pulmonary hemorrhage requiring transfusions, major/non-elective intervention, or was life-threatening; clinically significant postoperative wound healing complications; symptomatic congestive heart failure (CHF) responsive or refractory to intervention, and Reversible Posterior Leukoencephalopathy syndrome (RPLS), and (2) assess the incidence and types of "other" (i.e., not included in the list of select events) serious adverse events suspected by the investigator to be associated with Avastin use when combined with chemotherapy in the treatment of metastatic or locally advanced and unresectable CRC, locally advanced or metastatic non-small cell lung cancer (NSCLC), excluding predominant squamous histology, or locally recurrent or metastatic breast cancer.</p> <p><b>Technical Approach:</b> This is an observational study designed to follow patients with metastatic or locally advanced and unresectable CRC, locally advanced or metastatic NSCLC (excluding predominant squamous histology), or locally recurrent or metastatic breast cancer who are receiving Avastin in combination with first-line chemotherapy. Second-line metastatic CRC patients are also eligible. Patients who started their Avastin-containing therapy &lt; 3 months prior to enrollment are eligible. Patients with NSCLC or MBC will be eligible only after the FDA has approved the use of Avastin in those indications.</p>		

Data regarding prior adjuvant and/or additional lines of therapy will be collected for these

patients. The scope of the study will permit adverse events that occur infrequently with Avastin treatment (e.g., GI perforation) to be detected, analyzed, and described. In addition, the effectiveness of Avastin in a less selected, community-based population of first-line and second-line metastatic or locally advanced and unresectable CRC, locally advanced or metastatic NSCLC, or locally recurrent or metastatic breast cancer will be described. No study visits or evaluations will be required. Patients will be evaluated according to the physician's standard practice and discretion. Patient data will be drawn from the patients' medical records and reported by means of a web-based electronic data collection (EDC) system. Patients will be considered "on study" (including survival) for a maximum of three years or until death, withdrawal of consent loss to follow-up or study closure.

**Progress:** This protocol was initially approved by the Expedited Review Committee on 21 March 2007; however, contract negotiations between the study sponsor and the HMJF failed and the protocol was terminated on 24 April 2007, prior to receiving final approval.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207089	<b>Status:</b> Ongoing
<b>Title:</b> An international, randomised, double blind, placebo controlled, parallel group study to investigate whether TroVax, added to first-line standard of care therapy, prolongs the survival of patients with locally advanced or metastatic clear cell renal adenocarcinoma		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> pending - Jun 2012	<b>Funding:</b> Oxford BioMedica via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective of this study is to assess survival and adverse event rate in subjects receiving TroVax® vs placebo. Secondary objectives are (1) to compare the progression-free survival at 26 weeks, (2) to compare the tumor response rates and duration of response, (3) to assess whether the addition of the minimum of three doses of TroVax® to standard care will prolong survival when compared with placebo, and (4) to assess whether TroVax® has an impact on the quality of life as measured by QLQ30 and EuroQOL questionnaires.

**Technical Approach:** This is a Phase III, randomized, double blinded, placebo controlled study of TroVax® vaccine versus placebo in combination with chemotherapy for patients with locally advanced or metastatic clear cell renal adenocarcinoma. A total of 700 subjects will be enrolled at sites in the US, Russia and Eastern Europe. Up to four subjects will be enrolled at MAMC. Eligible subjects will be randomly assigned to the vaccine or placebo arm, to be given concurrently with chemotherapy. Three chemotherapy regimens are allowed with this protocol; however, Sunitinib is the only regimen that is considered acceptable as first-line therapy at MAMC. Sunitinib will be given as a daily oral dose, for four weeks on and two weeks off. Study vaccine will be administered at Weeks 1, 3, 6, 9, 13, 17, 21, 25, 33, 41, 49, 57 and 65. Subjects will receive at least three vaccine doses, and will continue on vaccine until withdrawn due to disease progression, experience unacceptable toxicity, withdraw consent or by are withdrawn by investigator discretion. Subjects who withdraw from treatment will be asked to sign a follow-up consent form, to agree to continued data collection on subsequent treatment and survival. Outcomes will be measured by CT scan at baseline and 26 weeks, and by survival, progression-free survival and adverse toxicity data.

**Progress:** This greater than minimal risk protocol was initially approved by the IRB on 24 April 2007, but final approval remains pending PI compliance with a stipulation to obtain services of an Institutional Biosafety Committee (required per protocol) and submission of a revised protocol summary page once an IBC has been contracted. On 15 November 2007, DCI was notified that the services of the Western IBC have been contracted and approval documents are being circulated to the appropriate people for signatures. It is anticipated that the protocol approval process will proceed and the study will be forwarded to CIRO once revised documents have been submitted to DCI.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207090	<b>Status:</b> Terminated
<b>Title:</b> A Randomized, Double-blind, Multicenter, Placebo-controlled Study of Adjuvant Lapatinib in Women with Early-Stage ErbB2 Overexpressing Breast Cancer		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> Terminated before final approval	<b>Funding:</b> Opulink Corp via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective is to determine whether adjuvant therapy with Lapatinib will improve disease-free survival in women with early-stage ErbB2-overexpressing breast cancer.

The secondary objectives are to evaluate and compare between treatment arms the following: overall survival; recurrence-free intervals {local, regional, distant, and central nervous system (CNS)}; the rate of CNS recurrence; toxicities; and quality of life, as physical and mental health status. In addition, a specific sub-study evaluating the effect of Lapatinib on QT/QTc interval will be conducted in selected centers in a subset of subjects. This study will assess relevant biomarkers and genetic changes in plasma and intra-tumoral samples and their correlation to both drug efficacy and clinical outcome.

The pharmacogenetic objective of the study is to investigate the relationship between genetic variants in candidate genes in the host and response (efficacy, safety, and tolerability) to Lapatinib. In addition, a specific sub-study comparing the transcriptional and protein profile of the archived tumor tissue sample to that of a tumor biopsy sample obtained at the time of the disease recurrence will be conducted.

**Technical Approach:** This is a randomized, double-blind, phase III adjuvant study to evaluate and compare the safety and efficacy of single-agent Lapatinib versus placebo in women with early-stage ErbB2-overexpressing breast cancer. Eligible women must have had an initial diagnosis of histologically/cytologically confirmed invasive breast cancer (Stage I through Stage IIIb) with ErbB2 over expression defined as 3+ by immunohistochemistry (IHC) or c-erbB2 gene amplification by fluorescence in-situ hybridization (FISH). Eligible women must have completed primary adjuvant chemotherapy; however, those with hormone receptor-positive disease may remain on endocrine therapy during the study. Eligible women must have no clinical or radiographic evidence of disease at the time of study entry.

**Progress:** This greater than minimal risk protocol received initial IRB approval on 24 April 2007; however, the PI submitted a termination memo dated 8 August 2007, prior to obtaining final approval. The time commitment required to provide administrative oversight for this protocol was felt to be too great, due primarily to the excessive number of external serious adverse event reports (over 300) already submitted on a monthly basis by the study sponsor.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207110	<b>Status:</b> Ongoing
<b>Title:</b> Micronics Protocol for Typing 'Waste' Blood Samples from Madigan Army Medical Center		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Anne L. Champeaux, MC; Carol D. Dean, MPH, BSN; CPT Abraham Loo, MC		
<b>Start - Completion:</b> 14 Aug 2007 - Jul 2008	<b>Funding:</b> Micronics via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this protocol is to supply de-identified ABO/Rh typing waste blood samples and typing results to Micronics for quality control testing of a prototype ABO/Rh Donor Screening Card.

**Technical Approach:** This protocol allows for the collection and shipping to Micronics of 300 to 400 waste ABO/Rh blood typing samples. Micronics will use these samples for an internal quality control study of a prototype ABO/Rh blood typing card designed for rapid point-of-care blood typing. Blood typing samples will be collected and shipped weekly from the Madigan Army Medical Center Pathology Laboratory to Micronics in Seattle. Samples and results will be stripped of identifiers and marked with a study sample number. A master list of the sample ID and study number will be maintained by the research office and will be destroyed at the end of the study. Results from the study may be shared with MAMC staff by Micronics at the end of the study.

**Progress:** This minimal risk protocol received final approval by the Expedited Review Committee, effective 20 July 2007, and CIRO approval on 14 August 2007. Collection and shipping of blood samples began immediately following CRADA/SOW approval, 11 September 2007.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205036	<b>Status:</b> Ongoing
<b>Title:</b> CTSU NSABP C-08, A Phase III Clinical Trial Comparing Infusional 5-Fluorouracil (5-FU), Leucovorin, And Oxaliplatin (mFOLFOX6) Every Two Weeks With Bevacizumab To The Same Regimen Without Bevacizumab For The Treatment Of Patients With Resected Stages II And III Carcinoma of the Colon		
<b>Principal Investigator:</b> MAJ Angela G. Mysliwiec, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC David E. McCune, MC; MAJ Jasmine T. Daniels, MC		
<b>Start - Completion:</b> 3 May 2005 - Mar 2009	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 3 Jan 2008

**Study Objective:** Primary Objective is to compare the relative efficacy of mFOLFOX6 + bevacizumab with that of mFOLFOX6 alone in prolonging disease-free survival (DFS). Secondary Objective is to compare the relative efficacy of mFOLFOX6 + bevacizumab with that of mFOLFOX6 alone in prolonging survival (S).

**Technical Approach:** Eligible subjects will be randomized into one of the two study groups. Patients in Group 1 will receive the drugs 5-FU, Leucovorin, and Oxaliplatin, repeated every 14 days (one cycle) for a total of 12 cycles of chemotherapy. Patients in Group 2 will receive 5-FU, Leucovorin, and Oxaliplatin, repeated every 14 days (one cycle) for a total of 12 cycles of chemotherapy and also receive bevacizumab on day 1 of each cycle before receiving the chemotherapy. After chemotherapy is done, subjects will continue to receive bevacizumab once every 2 weeks for another 6 months. Subjects will continue to be followed for the first 5 years with physical exams, urine and blood tests, and an enema with x-ray or endoscopic exam. National accrual is expected to be 2632 patients over 4 years. Investigators estimate approximately 4 patients per year for a total of 16 patients enrolled at MAMC.

**Progress:** This protocol closed to enrollment in October 2006, with four subjects enrolled at MAMC. One subject was reported on study treatment as of January 2007, two subjects in follow-up and the other subject chose to stop study treatment for personal reasons. The protocol remains ongoing to complete long term follow-up of enrolled subjects. Multiple external adverse events have been submitted. No changes to the protocol were reported during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207088	<b>Status:</b> Ongoing
<b>Title:</b> CTSU E2805, ASSURE: Adjuvant Sorafenib or Sunitinib for Unfavorable Renal Carcinoma		
<b>Principal Investigator:</b> MAJ Angela G. Mysliwiec, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Richard D. Reed, MC; LTC David E. McCune, MC		
<b>Start - Completion:</b> 24 Jul 2007 - Jul 2012	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective of this study is to demonstrate an improvement in disease-free survival in locally advanced renal cell (kidney) cancer patients randomly assigned to adjuvant Sunitinib (Arm A) or Sorafenib (Arm B) versus Placebo (Arm C) after radical or partial kidney removal.

Secondary objectives are to (1) compare overall survival of patients randomized to each of the two regimens with placebo, (2) further define the toxicity (side effects) of prolonged administration of Sunitinib or Sorafenib in this patient population, and (3) prospectively collect tumor and biological specimens to assess their characteristics and associations.

**Technical Approach:** After stratification by risk of relapse, ability to perform activities of daily living, cell type, and type of surgery, eligible, consenting subjects will be randomized to receive either: Arm A; Sunitinib, 50 mgs by mouth once a day times four weeks, followed by a two-week rest, for nine (six-week) cycles; and Placebo for Sorafenib by mouth twice a day times six weeks for nine (six-week) cycles. Arm B; Sorafenib, 400 mgs by mouth twice a day times six weeks for nine (six-week) cycles, and Placebo for Sunitinib by mouth once a day times four weeks, followed by a two-week rest, for nine (six-week) cycles. Arm C; Standard Arm - placebo for Sorafenib by mouth twice a day times six weeks for nine (six-week) cycles, and Placebo for Sunitinib by mouth once a day times four weeks, followed by a two-week rest, for nine (six-week) cycles.

**Progress:** This greater than minimal risk protocol was initially approved by the IRB on 24 April 2007, and final approval received on 24 July 2007. No subjects were enrolled during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 207097	<b>Status:</b> Ongoing
<b>Title:</b> CTSU CALGB 90401, A Randomized Double-Blinded Placebo Controlled Phase III Trial Comparing Docetaxel and Prednisone With and Without Bevacizumab (IND #7921, NSC #704865) in Men With Hormone Refractory Prostate Cancer			
<b>Principal Investigator:</b> MAJ Angela G. Mysliwiec, MC			
<b>Department:</b> Medicine/Hematology & Oncology			<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Richard D. Reed, MC; LTC David E. McCune, MC			
<b>Start - Completion:</b> 17 Aug 2007 - Jun 2012	<b>Funding:</b> SWOG via Henry M. Jackson Foundation		<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective of this study is to determine if the addition of bevacizumab to docetaxel and prednisone increases overall survival compared to docetaxel and prednisone alone in patients with HRPC.

Secondary objectives are to compare the (1) progression-free survival of these two regimens in patients with HRPC, (2) two regimens on the proportion of patients who experience a 50% post-therapy PSA decline from baseline, and (3) two regimens with respect to the proportion of patients who experience grade 3 or higher toxicities.

**Technical Approach:** This will be a randomized double blinded placebo controlled phase III trial with overall survival endpoint in patients with progressive hormone refractory prostate cancer. The blinded control arm will help eliminate investigator bias, which is critically important in drugs that may have cytostatic effects whose overall benefit will not be evident immediately. Because the FDA has approved docetaxel (75 mg/m<sup>2</sup>) along with twice a day oral prednisone 5 mg as the first line chemotherapy in HRPC, this will constitute the control arm. In this study, patients will be randomized to docetaxel 75 mg/m<sup>2</sup> IV repeated every 3 weeks plus prednisone 5 mg p.o. b.i.d. with either bevacizumab (15 mg/kg) IV or placebo every 3 weeks.

**Progress:** This greater than minimal risk protocol received initial IRB approval 22 May 2007. Final approval was received on 17 August 2007; protocol documents were released to the study staff on that date.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207098	<b>Status:</b> Ongoing
<b>Title:</b> CTSU NSABP B-42, A Clinical Trial to Determine the Efficacy of Five Years of Letrozole Compared to Placebo in Patients Completing Five Years of Hormonal Therapy Consisting of an Aromatase Inhibitor (AI) or Tamoxifen Followed by an AI in Prolonging Disease-Free Survival in Postmenopausal Women with Hormone Receptor Positive Breast Cancer		
<b>Principal Investigator:</b> MAJ Angela G. Mysliwiec, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC David E. McCune, MC; MAJ Jasmine T. Daniels, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 31 Oct 2007 - Jun 2012	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The main objective of this study is to determine if prolonged adjuvant hormonal therapy with Letrozole will improve disease-free survival in postmenopausal women with hormone receptor positive tumors who have completed five years of hormonal therapy with either 5 years of an aromatase inhibitor (AI) or up to 3 years of Tamoxifen followed by an AI.

Secondary aims of the study are to determine whether or not prolonged adjuvant Letrozole will improve survival, breast cancer-free interval, and distant recurrence; and increase the incidence of osteoporosis-related fractures and arterial blood clot events (such as strokes, heart attacks, etc.).

**Technical Approach:** This is a phase III randomized, double-blind study. Eligible patients who have received five years of adjuvant hormonal therapy will be randomized to either Group 1 (placebo by mouth once a day for 5 years) or Group 2 (Letrozole 2.5mg by mouth once a day for 5 years). Patients will be stratified by lymph node involvement (yes/no); Tamoxifen as adjuvant therapy (yes/no); and bone mineral density (osteoporosis) score.

This study includes an optional Letrozole registration program (sub-study) for patients who have not yet completed five years of initial adjuvant hormonal therapy. In order to have a predominantly Letrozole-treated population, patients who have taken a minimum of two years of hormonal therapy with Tamoxifen or an AI may be offered Letrozole.

**Progress:** This greater than minimal risk protocol received initial IRB approval 22 May 2007. Final approval was received 31 October 2007; protocol documents were released to the study staff on that date.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204082	<b>Status:</b> Completed
<b>Title:</b> Evaluating Cognitive Function in Women Receiving Chemotherapy for Newly Diagnosed Breast Cancer		
<b>Principal Investigator:</b> Margaret J. Ramsdell, RN, BSN, OCN		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Donna L. Berry, Ph.D., RN		
<b>Start - Completion:</b> 25 May 2004 - Oct 2004	<b>Funding:</b> DCI	<b>Periodic Review:</b> 22 May 2006

**Study Objective:** To evaluate cognitive function in women newly diagnosed with breast cancer, receiving chemotherapy and the effect of cognitive function on the individual's quality of life. This study will examine both the relationship between cognitive function scores and patient's self-reported cognitive problems and the meaning of the measures for women receiving chemotherapy for breast cancer. Specifically: (1) to describe function scores of the EORTC QLQ C-30 cognitive subscale and the High Sensitivity Cognitive Screen (HSCS) in women with breast cancer at baseline and mid point in chemotherapy treatment for breast cancer, and (2) to evaluate the process and meaning of answers on the HSCS and the cognitive subscale questions of the EORTC QLQ C-30 questionnaire.

**Technical Approach:** This study will utilize a longitudinal, pre-post test design to evaluate women newly diagnosed with breast cancer who will be receiving doxorubicin and cyclophosphamide. Women ages 25-70, newly diagnosed with breast cancer will be asked to participate in this study. Subjects interested will fill out a 3x5 card with name and phone number and will be contacted by the PI. After signing consent and answering questions, patients will fill out the EORTC QLQ C-30 questionnaire. Upon completion of the EORTC QLQ C-30 a cognitive interview of those questions will be conducted to find out how the subjects felt about reading and answering the questions, what those questions mean to them and how their cognitive function currently is affecting their quality of life. The HSCS, a sensitive tool for detecting subtle cognitive impairment, will be administered at the completion of the cognitive interview. Descriptive statistics will be used to summarize the demographic characteristics of the EORTC QLQ C-30 cognitive scale scores and the cognitive domain scores on the HSCS of the subjects of two time points per chemotherapy and at mid point during chemotherapy. The Mann-Whitney test will be used to compare cognitive scale scores on the EORTC QLQ C-30 and cognitive domain scores on the HSCS in subjects at the same time point. The results at both time points will be graded and examined for changes in scores on the HSCS as well as changes in the five item subscale of the EORTC QLQ C-30.

**Progress:** This protocol was reported as completed in May 2007. Six subjects were enrolled and completed both testing points of this study. It was found that mild cognitive dysfunction was evident at base line and the majority of patients have some mild cognitive dysfunction at the second testing point. Based on the results from the cognitive interviews the major theme was that patients were not able to remain focused when completing daily tasks.

### Detail Summary Sheet

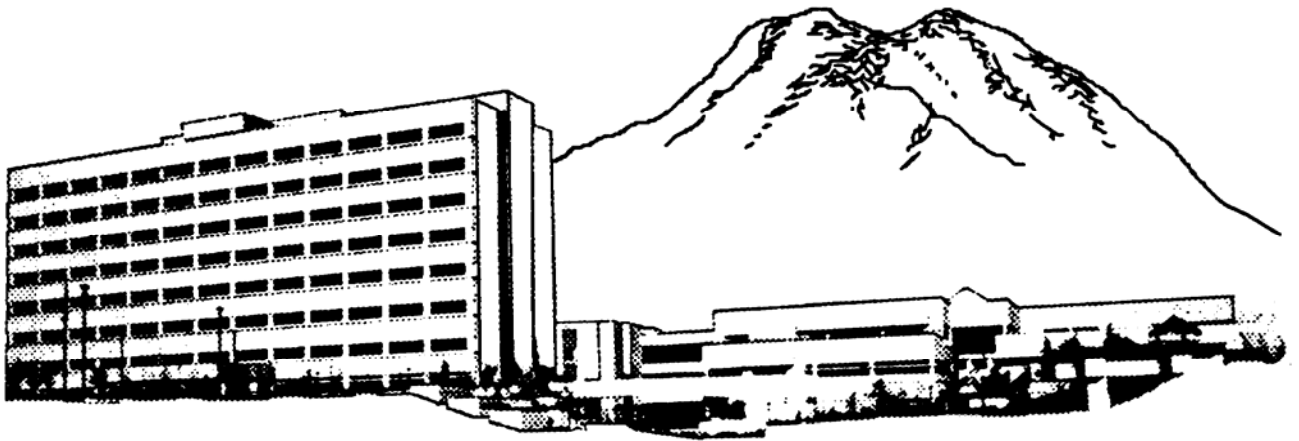
<b>Date:</b> 30 Sep 07	<b>Number:</b> 206113	<b>Status:</b> Ongoing
<b>Title:</b> CTSU E5202: A Randomized Phase III Study Comparing 5-FU, Leucovorin and Oxaliplatin versus 5-FU, Leucovorin, Oxaliplatin and Bevacizumab in Patients with Stage II Colon Cancer at High Risk for Recurrence to Determine Prospectively the Prognostic Value of Molecular Markers		
<b>Principal Investigator:</b> LTC James A. Sebesta, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Tommy A. Brown, MC; MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; LTC David E. McCune, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 28 Nov 2006 - Aug 2011	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 25 Jun 2007

**Study Objective:** The primary objective of this study is to demonstrate an improvement in 3-year disease-free survival for high risk stage II colon cancer patients randomly assigned to 5-FU, leucovorin, and oxaliplatin (FOLFOX) versus FOLFOX plus bevacizumab.

Secondary objectives of this study are to: Compare overall survival between regimens; further identify the toxicities of the regimens; prospectively determine the impact of tumor biological characteristics on the survival of patients with stage II colon cancer.

**Technical Approach:** In this study, patients determined to be high-risk by the molecular analysis will receive chemotherapy +/- bevacizumab. A total of 3610 patients will be enrolled in this study, with up to 10 patients per year enrolled at MAMC. Baseline assessment will include history and physical, vitals and performance status, CBC, Chemistry, LFTs, CEA, PT, PTT, INR, urine protein/creatinine (UPC) ratio, and serum pregnancy test if applicable. All eligible, consenting participants will have a block of resected tumor sent to a central lab for biology-based risk assessment. Patients found to be low risk, will be registered to Arm C, the observation arm. Patients found to be high risk, will be randomized to receive either: ARM A (control arm): 5-FU, leucovorin, and oxaliplatin (FOLFOX regimen) IV every 2 weeks x 12 or ARM B: FOLFOX plus bevacizumab IV every 2 weeks x 12, followed by bevacizumab alone for 12 additional treatments (IV every 2 weeks). Patients will be followed every 3 months for 2 years, every 6 months for Year 3 through Year 5, and then every 12 months thereafter for a total of 10 years. Follow-up will include physical exam, performance status, CEA, and colonoscopy and biopsy where indicated.

**Progress:** This greater than minimal risk protocol received final approval on 28 November 2006. The study remains open to enrollment with no subjects were screened or enrolled during FY07.



## **Detail Summary Sheets**

Infectious Disease Service, Department of  
Medicine

### Detail Summary Sheet

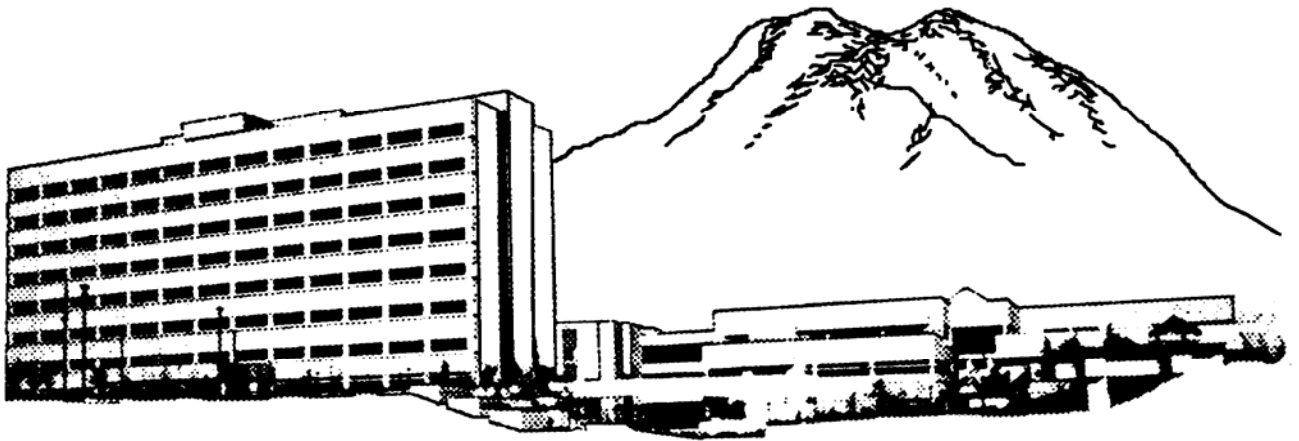
<b>Date:</b> 30 Sep 07	<b>Number:</b> 207123	<b>Status:</b> Ongoing
<b>Title:</b> Improving Patient Outcomes Using a Collaborative Hypertension Clinic		
<b>Principal Investigator:</b> CPT Ramesh G. Venkataraman, MC		
<b>Department:</b> Medicine/Infectious Disease		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Jon C. Allison, MC; COL Howard M. Cushner, MC; CPT Sean C. Reilly, MC; Emily V. Leaf, PharmD; Helen S. Booth, PharmD		
<b>Start - Completion:</b> 10 Sep 2007 -	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this protocol is to study the effectiveness of a multidisciplinary hypertension clinic in achieving blood pressure goals in patients with uncontrolled hypertension.

**Technical Approach:** This is a retrospective chart review; data will be collected from records generated between 1 May 2005 and 30 April 2007 on individuals enrolled in the hypertension clinic between 1 May 2005 and 31 October 2006. This data will then be represented graphically with confidence intervals for analysis and interpretation. Ultimately, if the data supports significant benefit to hypertensive patients, this clinic could serve as a model for similar ventures at other medical institutions.

**Progress:** This minimal risk protocol received final approval by the Expedited Review Committee, effective 10 September 2007.





## **Detail Summary Sheets**

Internal Medicine Service, Department of  
Medicine

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 202048	<b>Status:</b> Ongoing
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**Title:** A Multinational, Randomized, Double-blind, Placebo-controlled, Forced-titration, 2X2 Factorial Design Study of the Efficacy and Safety of Long Term Administration of Nateglinide and Valsartan in the Prevention of Diabetes and Cardiovascular Outcomes in Subjects with Impaired Glucose Tolerance (IGT), Protocol No. CDJN608 B2302

**Principal Investigator:** LTC Jon C. Allison, MC

<b>Department:</b> Medicine/Internal Medicine	<b>Facility:</b> MAMC
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**Associate Investigator(s):** MAJ Patricia A. Short, MC; Shaila B. Kode, M.D.; Marvin Y. Hayami, M.D.; LTC Cecily K. Peterson, MC

<b>Start - Completion:</b> 19 Apr 2002 - Aug 2009	<b>Funding:</b> Novartis via Henry M. Jackson Foundation	<b>Periodic Review:</b> 27 Feb 2007
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**Study Objective:** Core Phase: to evaluate the effect of long-term administration of nateglinide and valsartan on the progression to diabetes in subjects with impaired glucose tolerance (IGT) at increased risk of a cardiovascular event. Extension Phase: to evaluate the effect of long-term administration of nateglinide and valsartan on cardiovascular morbidity and mortality. Definition of this composite endpoint is provided on page 11 of the attached Protocol, and is further discussed in the Summary to this cover document.

**Technical Approach:** Approximately 24 subjects will be enrolled at MAMC. Study design projects enrollment of 7500 subjects from 600-800 centers in about 40 countries, with approximately 1875 subjects in each of 4 treatment groups. 75% of subjects will receive at least one of the study drugs. All study drugs are taken orally. Patients will be invited to participate in screening who have one or more risk factors for the conditions under study (such as family history, known IGT, high BMI, dyslipidemia.) Eligible patients will be randomized into one of four groups (1. Nateglinide 60 mg before meals + matching placebo once daily; 2. Nateglinide 60mg before meals + Valsartan 160mg once daily; 3. Matching placebo before meals + matching placebo once daily; 4. Matching placebo before meals + Valsartan 160mg once daily) using an electronic interactive voice recognition system. There will be sixteen study visits after initiation of study treatment: at +2 weeks, +4 weeks, +3 months, +6 months, then visits will be every 6 months. Patients will arrive fasting, scheduled between 7-10am. Weight, blood pressure, heart rate and blood sampling is performed at each visit. A urine specimen will be collected at 3 time points. An ECG, (electrocardiogram) is performed at the second visit and repeated twice during the study. The OGTT with FPG and insulin level is completed every 12 months after baseline, at month 37(for confirmation), and as indicated to confirm progression to diabetes. Subjects are asked to keep a diary of suspected hypoglycemic events and a subset of patients may be provided a blood glucose monitor to record these occurrences. This study will include life style intervention counseling of subjects at every visit, with written educational materials provided by the study sponsor.

**Progress:** This protocol closed to patient entry 26 November 2003, with five subjects enrolled. Three subjects continued to be followed at MAMC during FY07. Four external serious adverse events were reported. MAJ Short was approved as an interim PI for COL Allison for a period of time during FY07; otherwise, no changes to the protocol were submitted.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 204045	<b>Status:</b> Ongoing
<b>Title:</b> A Prospective, Multinational, Multicenter Trial to Compare the Effects of Amlodipine/Benazepril to Benazepril and Hydrochlorothiazide Combined on the Reduction of Cardiovascular Morbidity and Mortality in Patients With High Risk Hypertension. Protocol No. CCIB002I2301: ACCOMPLISH (Avoiding Cardiovascular Events through COMbination Therapy in Patients Living with Systolic Hypertension)			
<b>Principal Investigator:</b> LTC Jon C. Allison, MC			
<b>Department:</b> Medicine/Internal Medicine			<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Patricia A. Short, MC; Michael R. Voorhies, PAC			
<b>Start - Completion:</b> 7 Apr 2004 - Oct 2009	<b>Funding:</b> Novartis via Henry M. Jackson Foundation		<b>Periodic Review:</b> 27 Feb 2007
<b>Study Objective:</b> (1) To assess the time to first event of composite cardiovascular morbidity and mortality with amlodipine/benazepril (Lotrel®) compared with the combination of benazepril and hydrochlorothiazide in patients with high risk hypertension. (2) To compare composite cardiovascular morbidity, new onset diabetes, progression of renal disease and hospitalization for congestive heart failure with amlodipine/benazepril (Lotrel®) versus the combination of benazepril and hydrochlorothiazide. (3) to compare all-cause mortality, all hospitalizations, renal function (estimated change in glomerular filtration rate), LVH, peripheral arterial revascularization procedure or nontraumatic amputation and progression/regression of microalbuminuria (30-300 mg/g) or clinical albuminuria (>300 mg/g) long term safety and tolerability with amlodipine/benazepril (Lotrel®) versus the combination of benazepril and hydrochlorothiazide. (4) To identify inherited genetic factors which may be related to hypertension, predict response to treatment with the study medications, predict relative susceptibility to drug-drug interactions, or predict genetic predisposition to serious side effects.			
<b>Technical Approach:</b> This is a phase III randomized, multicenter, double-blind, parallel-group, active-controlled trial comparing the efficacy of amlodipine/benazepril combined therapy (Lotrel) to the combination of benazepril and hydrochlorothiazide (HCTZ) in high risk hypertensive subjects in reducing cardiovascular outcomes. 20 subjects may be enrolled at MAMC with approximately 12,600 worldwide. The study will last approximately 5 years, including the 18-month recruitment period. Eligible subjects will be randomized in 1:1 ratio to one of two groups to begin blinded treatment with amlodipine/benazepril 5/20 mg or benazepril 20mg/HCTZ 12.5 mg. The study provides for dose-titration followed by add-on therapy if necessary to achieve goal blood pressure (<140/<90 mmHg or lower in appropriate subjects).			
Subjects will be followed every 4 weeks up to 3 months, at 6 months, and every 6 months thereafter. All randomized subjects will be followed until study completion, including those who interrupt or discontinue treatment. Additional visits may be done as needed to ensure blood pressure control. Patients will be treated in the study until the required number of randomized subjects with a primary cardiovascular event is achieved for analysis. Safety and efficacy assessments will consist of monitoring pre-defined non-serious adverse events, all serious adverse events, concomitant medications, regular monitoring of hematology and blood chemistry, urinalysis, vital signs and physical examinations. Observation for clinical endpoints will be continuous. Physical exams will focus on cardiovascular signs and symptoms. 12-lead ECG will be performed at baseline, month 18 and year 3. 24-hour ambulatory blood pressure monitoring at Year 2 will be done in a subset of subjects. Biomarker tests for high sensitivity C-reactive protein and other predictors of cardiovascular disease are scheduled. Subject participation in a pharmacogenetics sub-study is optional. A single blood specimen will be collected and DNA derived from the sample may be stored and studied for up to 20 years by the study sponsor. Interim analyses for monitoring of efficacy demonstration and patient safety will be conducted by an			

independent Data Monitoring Committee.

**Progress:** This protocol closed enrollment in December 2005, with 28 subjects consented; seventeen enrolled. Three subjects discontinued taking study medication; all seventeen continue to be followed. MAJ Short was approved as an interim PI for COL Allison for a period of time during FY07. A protocol deviation was reported when it was discovered that a subject took a concomitant medication that is not allowed per protocol, prescribed by primary health care physician who was not aware of the protocol's restricted medications. Multiple internal adverse events have been reported at subject's one year study visit, along with several external adverse event reports. Amendment #4 and #5 changes to the protocol were submitted; Amendment #5 is scheduled for IRB review in December 2007. The protocol remains ongoing to complete follow-up study visits.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205046	<b>Status:</b> Terminated
<b>Title:</b> The Effect of Blood Transfusion on Serum Ferritin and Iron		
<b>Principal Investigator:</b> CPT Corinna Avalos, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Daniel G. Cuadrado, MC; COL Ronald H. Cooper, MC; LTC Rajat Bannerji, MC; CPT Ashley A. Feaver, MC; CPT Patrick M. McNutt, MS		
<b>Start - Completion:</b> 26 May 2005 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 24 Jan 2006

**Study Objective:** To study the effect of packed red blood cell transfusion on ferritin level and iron panel.

**Technical Approach:** In this descriptive study a database containing demographic and medical information will be constructed for patients who have anemia requiring non-emergent packed red blood cell transfusions. Candidates for the study will be identified by a list of excluding medical conditions a physician will go through prior to the transfusion and consent. Eligible patients who consent to the study will have their iron panel and ferritin levels drawn prior to transfusion and six other times as specified after transfusion.

**Progress:** No work was conducted on this protocol during FY07. The protocol was terminated as only four evaluable subjects enrolled while the study was active, out of the 50 subjects required for statistical analysis.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205123	<b>Status:</b> Ongoing
<b>Title:</b> Current Use and Complications of Peripherally Inserted Central Catheters (PICC): A Retrospective Study		
<b>Principal Investigator:</b> CPT Kathleen C. Bauler, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Joel T. Abbott, MC; LTC Alexander S. Niven, MC; LTC Cecily K. Peterson, MC		
<b>Start - Completion:</b> 18 Aug 2005 - Jun 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 22 Jan 2008

**Study Objective:** Evaluate the indications for placement, duration of therapy and complications of peripherally inserted central catheters (PICC) lines in the inpatient population at Madigan Army Medical Center.

**Technical Approach:** This is a retrospective chart review of consecutive inpatients with PICC lines as identified from PICC service records. Subjects without documentation of a minimum of one endpoint will be excluded from further analysis and recorded by clinical service as "no data available." A data sheet will be completed for subjects with a minimum of one recorded end point (PICC line placement, removal or "unknown" re: PICC). Each subject's demographics, pertinent medical history, indication, duration, and complications of PICC line placement, nurse placing PICC line and years of experience will be recorded. 100 consecutive subject's charts will be reviewed using this criterion. Primary variables will be indication, duration of therapy, and complications. Subjects with and without complications will be separated and analyzed by indication, duration of therapy, demographic and medical information, and nursing information. Data will be analyzed using Chi-squared, ANOVA and MANOVA analysis.

**Progress:** During FY 2007, there have been approximately 20-25 charts reviewed out of the 100 charts request. No data analysis has been conducted on the preliminary data obtained. CPT Bauler was not able to complete the protocol prior to leaving MAMC. Work on this study was formally suspended in August 2007, pending submission of a change in the role of PI and completion of the continuing review process.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206069	<b>Status:</b> Ongoing
<b>Title:</b> The Effects of Nighttime Low Dose Aspirin on Ambulatory Blood Pressure Testing in Treated Hypertensive Patients		
<b>Principal Investigator:</b> MAJ Herbert P. Kwon, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Mark E. Smith, MC; MAJ Jason L. Davis, MC		
<b>Start - Completion:</b> 12 Jun 2006 - Dec 2006	<b>Funding:</b> Spacelabs via DCI	<b>Periodic Review:</b> 27 Mar 2007

**Study Objective:** To determine the benefits of aspirin chronotherapy in patients already on anti-hypertensive therapy.

**Technical Approach:** Eligible patients who consent to participate will have a baseline physical exam performed that will include a cardiovascular exam. If signify underlying occult organic heart disease is detected the patient will not be included in the study. If the work up is negative, the patient will be included in the study. After an evening of fasting, patients will have six blood pressure measurements taken after sitting for at least 5 minutes. All efforts will be made to ensure the measurements are taken on the same type of machine by the same individual, and at the relatively same times in the morning (between 0800 and 1100). Patients will be randomly assigned to either remain on their aspirin in the morning or to take it nightly. Patients will then have physical measurements taken and their fasting blood drawn. Finally, a Spacelabs 90207 Ambulatory Blood Pressure Monitor {ABPM} (Issaquah, Washington) will be placed and instructions for use given.

Ambulatory Blood Pressure Monitor: Patients will have blood pressure and heart rates measured every 20 minutes between 0700 and 2300 if they are civilian and 0600 and 2200 if they military participants. During the eight hour "rest period" patients will have measurements taken every 30 minutes. Data will not be used if there is >30% of measurements missing, data missing for more than 2 hours, or if patients fail to return for a second ambulatory blood pressure measurement. After returning the blood pressure monitor, patients will receive a new bottle of aspirin with a sticker stating if the medication should be taken in the morning or evening in addition to the normal written instructions, which will conclude initial randomization to a study arm. Investigators will be blinded to the timing of aspirin administration. Measurements will be submitted via email at Months 0-3 (First Inter-measurement Period), Month 3 (Interim Evaluation) and Months 4-6 (Second Inter-measurement Period. Patients will have the timing of their low dose aspirin reversed, serving as their own controls and cross-overs. Participants who took it in the evening will now take it in the morning and vice versa. Patients will be contacted, encouraged to stay consistent with the protocol, and/or to contact Dr. Kwon or study staff. The values obtained for the ABPM and the fasting labs at the interim evaluation above will be used also for the baseline for the second inter-measurement period.

**Final Evaluation:** After the final three months of therapy patients will return for a fasting laboratory sampling, appointment and re-measurement of blood pressure to include another 48 hour AMBP. Medical records will be reviewed for any interim visits, hospitalizations, or medication changes. Patients will be asked if they suffered any increase in side effects or gastrointestinal discomfort during the study period.

**Progress:** This greater than minimal risk protocol received final IRB approval on 12 June 2006. Five subjects enrolled in the initial phase of the study during FY07. There have been no withdrawals and no reported adverse events. Enrollment continues, but has been extremely difficult due to an inability to enroll diabetic patients.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206087	<b>Status:</b> Completed
<b>Title:</b> Hemoptysis in Young Adults		
<b>Principal Investigator:</b> MAJ Herbert P. Kwon, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Vincent Mysliwiec, MC		
<b>Start - Completion:</b> 8 May 2006 - Aug 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To report in case series format the causes of hemoptysis in young adults as determined by bronchoscopy at the MAMC Pulmonary clinic in a retrospective medical record review.

**Technical Approach:** A retrospective chart review will be performed utilizing the MAMC Pulmonary Clinic Bronchoscopy logbook as the initial source of patient identification. The logbook for the years of 2000-2006 will be screened for individuals undergoing bronchoscopy within the age range of 18 through 45 years of age. The indication for bronchoscopy will be screened for hemoptysis.

**Progress:** This protocol was completed during FY07. There were 18 patients, ages 19-42, 16(89%) active duty, 14(78%) male, and 12(67%) non-smokers. The diagnoses included 4(22%) cancers, 4(22%) cases of bronchitis, 3(17%) cases of pneumonia, 1(6%) case of medication side effect, and 1(6%) case of obstructive sleep apnea. In 5 patients there was no etiology identified and no bleeding visualized on bronchoscopy. All six patients with cancer or pneumonia had abnormal chest roentgenograms (CXR) and/or computerized tomography (CT). All nine patients with bronchitis or an unidentified etiology had non-massive hemoptysis, normal CXRs and normal CT (if it was performed). None of the 5 cases with unknown etiologies had a recorded recurrence or etiology identified. Conclusions: In our population, bronchoscopy in the setting of non-massive hemoptysis with a normal CXR and CT of the chest did not find any unsuspected endobronchial abnormalities. A Poster from this study took second place at Army ACP Chapter meeting November 2006. A Poster was accepted for National ACP poster competition April 2007. A manuscript has been submitted to the Journal of Bronchoscopy April 2007 and is currently under review.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205039	<b>Status:</b> Completed
<b>Title:</b> Management of Parapneumonic Effusions: Does Following Pneumonia Treatment Guidelines Affect Outcome? A Retrospective Study		
<b>Principal Investigator:</b> CPT Patricia Papadopoulos, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Bernard J. Roth, MC; John G. Meyer, MD, MPH; MAJ John P. Rinard, MC		
<b>Start - Completion:</b> 11 Feb 2005 - Aug 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 16 Jan 2007

**Study Objective:** To determine whether pneumonia treatment guidelines are being followed at Madigan Army Medical Center in managing parapneumonic effusion and whether outcome is affected via retrospective chart review.

**Technical Approach:** This is a retrospective study of parapneumonic effusions in patients with the diagnosis of community-acquired pneumonia (CAP). Adult patients (age 18 years and older) that meet the diagnosis of pneumonia will be studied to determine whether a parapneumonic effusion (PPE) was present at time of diagnosis and if pneumonia management guidelines published by the IDSA and ATS were followed. If a PPE was present on chest radiograph, was a lateral decubitus study or CT scan then done? If the PPE layered >10 mm on lateral decubitus radiograph, was thoracentesis done? Did it change patient management and was outcome affected? If no difference of outcome is found, should the pneumonia management guidelines be updated? This study will look at patients given the diagnosis of CAP during the time frame from 01 Jan 02 to 31 Dec 03.

**Progress:** The manuscript of this retrospective study has been rejected by both the American Journal of Respiratory & Critical Care Medicine and CHEST. It was recently submitted to Archives of Internal Medicine on October 8th, 2007 and is still pending review. Results: 684 patients with CAP were identified. Of those, 72(10.5%) had radiographic evidence of a new effusion, and 27 of these 72(37.5%) underwent further imaging and management as suggested by the ATS guidelines. The complication rate was 3.6% in the 612 patients without effusions and 23.6% in the 72 patients with effusions ( $p < 0.001$ ). The complication rate was 21% in the 48 patients with effusions in whom the ATS guidelines were not followed and 21% in the 24 patients in whom the guidelines were followed ( $p = 1.0$ ).

**Conclusions:** This study confirms that the presence of a parapneumonic effusion is associated with a significant (6-fold) increase in the rate of complications in patients with CAP. Adherence to recommended ATS guidelines in this population did not result in a reduction in the complication rate.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207060	<b>Status:</b> Ongoing
<b>Title:</b> Effect of Combination Treatment with Fluticasone/Salmeterol (Advair) and Tiotropium (Spiriva) on Pulmonary Function Tests, Hospital Admissions, and Documented Exacerbations of COPD at MAMC		
<b>Principal Investigator:</b> CPT Jason E. Sapp, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Vincent Mysliwiec, MC; David J. Tomich, DAC		
<b>Start - Completion:</b> 12 Feb 2007 - Mar 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objectives are to (1) determine if combination therapy with Advair and Spiriva in COPD improves FEV1, FVC, and FEV1/FVC on follow-up pulmonary function tests compared to single agent therapy, and (2) determine if Advair/Spiriva combination therapy in COPD decreases rates of hospitalization or exacerbations of this condition.

**Technical Approach:** Addressing all pathophysiological facets of COPD involves utilizing medication that addresses both reversible airway obstruction and inflammation. In patients with severe or very severe COPD, this involves using both long-acting bronchodilators and inhaled corticosteroids. This study looks retrospectively at patients on single agent therapy, Fluticasone Propionate/Salmeterol (Advair) or Tiotropium Bromide (Spiriva), or combination therapy with both agents and comparisons between these two groups in post-treatment PFTs (FEV1, FVC, and FEV1/FVC), rates of hospital admissions, and documented exacerbations of COPD. 92 total patients were identified in both the outpatient and inpatient settings with a diagnosis of COPD on single agent or combination therapy who also have PFTs on record at MAMC. Their records will be reviewed during this study to determine if combination therapy is superior to therapy with a single agent and if this should be recommended as standard therapy for severe or very severe COPD at MAMC.

**Progress:** This minimal risk protocol received initial approval by the Expedited Review Committee on 12 February 2007. Protocol was amended to add Ms. McKay as technical staff. A progress report has not yet been requested.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206119	<b>Status:</b> Ongoing
<b>Title:</b> Urinary Markers of Renal Injury and N-Acetylcysteine Efficacy (URINE)		
<b>Principal Investigator:</b> CPT Mehdi C. Shelhamer, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jason L. Davis, MC; COL Howard M. Cushner, MC; CPT Nathan R. Evans, MC		
<b>Start - Completion:</b> 18 Oct 2006 - Mar 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 25 Sep 2007

**Study Objective:** The objective of this study is to attempt to measure NAC's effect at the renal tubular cell level by measuring two known markers for renal cell injury after a contrast load. A secondary objective will be to look into differences in these urinary enzyme levels based on how much IV contrast volume was given in both the study and control groups.

**Technical Approach:** Up to 90 patients who have been scheduled for a radiologic imaging study with IV contrast or heart catheterization will be recruited for this study. An additional 45 patients scheduled for a non-invasive imaging study such as an ultrasound will also be recruited. The goal is to enroll 135 patients who complete the study. Patients will be stratified by age (<50 and >50) and creatinine clearance (60-90 versus >90) as calculated by the MDRD equation<sup>20</sup> using a completed chem 7 or 14. The patients undergoing a heart catheterization or IV radiologic imaging study will be randomized to either NAC or no NAC using a computer program based on random number generation. NAC will be administered in 4 ounces of orange juice and control patients will receive an equivalent volume of normal saline (as NAC), also in 4 ounces of orange juice. Patients will be blinded to treatment and questioned as to which treatment they believe they received after the first dose and at the end of the study. 45 patients will be enrolled in a study group receiving NAC prophylaxis for their contrast study. 45 patients will serve in a control group, which will not receive NAC. The study will remain open until 45 patients are enrolled in each group. GGT and NAG will be measured from urine collections prior to the administration of NAC and contrast and 24 hours after the administration of contrast. A 50 cc spot urine specimen will be collected on all patients prior to taking the first dose of NAC. A second 50 cc spot urine specimen will then be collected 24 hours after the contrast study. Both urine specimens will be used to measure urine GGT and NAG levels standardized per gram of urine creatinine. The age, race, sex, baseline MDRD GFR, presence of diabetes, use of ACE inhibitor and amount of IV contrast volume given to each patient will also be recorded. Only the IND pharmacist will be aware of whether NAC is given to the patient (via computer generated randomization). Patients and investigators will be blinded as to who will receive NAC.

**Progress:** A change in the role of PI from CPT Evans to CPT Shelhamer was approved in October 2007. Nine subjects have enrolled. Enrollment has been slower than initially expected and recruitment of subjects continues. No significant adverse events reported. The associated protocol #207021 is progressing.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207021	<b>Status:</b> Ongoing
<b>Title:</b> Variation of Urinary Enzymes Gamma-Glutamyltransferase and N-Acetyl-Beta-D-Glucosaminidase in Patients Receiving N-Acetylcysteine		
<b>Principal Investigator:</b> CPT Mehdi C. Shelhamer, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jason L. Davis, MC; COL Howard M. Cushner, MC; CPT Nathan R. Evans, MC		
<b>Start - Completion:</b> 18 Jan 2007 - Jun 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 23 Oct 2007

**Study Objective:** The objective of this study will be to measure N-acetylcysteine's (NAC) effect at the renal tubular cell level by measuring two known markers of nephrotoxicity. This will be done by measuring urinary GGT (gamma- glutamyltransferase) and NAG (N- acetyl- beta -D- glucosaminidase) before and after the administration NAC.

**Technical Approach:** Patients routinely followed in the Internal Medicine, Nephrology and Cardiology clinics will be recruited and stratified by age (<50 and >50) and creatinine clearance (60-90 vs. >90) as calculated by the MDRD equation using completed chemistry panels. Subjects will be receiving four equal oral doses of NAC administered in four ounces of orange juice. A 50 cc spot urine specimen will be collected on all patients prior to taking the first dose of NAC. A second 50 cc spot urine specimen will then be collected twelve hours after the final dose of NAC. Both urine specimens will be used to measure urine GGT and NAG levels standardized per gram of urine creatinine. The age, race, sex, NSAID use, antibiotic use in last four weeks, statin use, ACE inhibitor use (and dose changes in last four weeks), diuretic use, presence of hypertension, diabetes or coronary artery disease and baseline MDRD GFR will be recorded for each patient. Once data has been obtained, statistical analysis will be undertaken to help determine whether NAC has a direct impact on the measurement of urinary NAG and GGT.

**Progress:** This greater than minimal risk protocol was initially approved by the IRB, 21 November 2006, and received final approval on 18 January 2007. Subject enrollment is going well with 25 subjects who have completed the study. An interim analysis will soon be conducted while subject enrollment continues. No adverse events have occurred.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207107	<b>Status:</b> Ongoing
<b>Title:</b> Geriatric Home Visit Program for Uniformed Services University MS3 students during their Internal Medicine Ambulatory Clerkship		
<b>Principal Investigator:</b> MAJ Patricia A. Short, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 13 Jul 2007 - 07/08	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The specific aims of this project are to see if a geriatric home visit changes student attitudes towards geriatrics patients and if a geriatrics home visit program augments student knowledge of geriatric syndromes.

**Technical Approach:** A geriatric home visit will ultimately be incorporated into the curriculum for the Uniformed Services University (USU) students as part of their third year Internal Medicine Clerkship. This is anticipated to occur in the 2008 academic year. As part of the pilot program and to study the impact, the geriatric home visit will be offered during the orientation to USU third year medical students who are rotating at MAMC as part of their ambulatory Internal Medicine clerkship during the 2007 academic year. Students who choose to participate will identify a patient from their clerkship experience to visit at home. Participating students will take a pretest, study geriatrics content on a multimedia CDROM and then visit the patient in their home. Each participating student will write a reflective paper based on their experience and will take a post-test after the visit. Study staff anticipates participation from five to ten students during the 2007-2008 academic year. This program has already been implemented and is being conducted in the national capital area with prior approvals from IRBs at NMMC, WRAMC and USU. The control group is being recruited at another site (Wilford Hall Medical Center) under their IRB approval. These students will be given the CDROM without instructions, complete the pre-test and the post-test, but not the home visit. The pretest and post test are based on prior research at other institutions, and are designed to measure the effect of the geriatrics home visit program on attitudes towards elderly patients, home care, and knowledge acquisition. The primary objective of the study is to compare the difference between pre- and post-test scores between intervention and control groups. Overall comparison of the total intervention group to the total control group will be the primary outcome, and secondary outcomes will compare the ambulatory and ward intervention groups to the ambulatory and ward control groups respectively. In addition, qualitative analysis will be performed of the write-ups generated by students in the intervention group to look for secondary goals of the project. Qualitative analysis is, by definition, a method of exploring collected information to identify themes.

**Progress:** This minimal risk protocol received final approval by the Expedited Review Committee, effective 13 July 2007.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207108	<b>Status:</b> Ongoing
<b>Title:</b> The Impact of Electronic Evaluation Systems on the Quality of Resident Evaluations		
<b>Principal Investigator:</b> MAJ Patricia A. Short, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 13 Jul 2007 - Jun 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objectives are to determine whether the quality and/or quantity of written comments about Internal Medicine residents changes after implementing an electronic system for collecting end of month rotations, and whether there is increased discrimination of evaluations to differentiate ratings of high levels of learners by demonstrating an increase in the variance of numeric evaluations after the implementation of an electronic evaluation system.

A secondary objective is to determine whether there is a correlation between the numeric rating scores in the 9 domains assessed in the ABIM forms and the quality of the written comments; and whether that correlation is uniform across all domains or is more likely to reflect a subset of the domains.

**Technical Approach:** The data to be collected from each site will be existing records about Internal Medicine residents who have either completed or are still in their Internal Medicine residency training. The data for the two years prior to the implementation of the electronic evaluation system will be paper-based end of month evaluation forms. The forms collected at each site will be copied, then coded and stripped of unique identifiers. Codes will be assigned to each resident, and each attending physician who completed the evaluation form, so their ratings can be correlated longitudinally, but once each form has been assigned a code, the code book will be destroyed, ensuring anonymity of any individual in the database. Additional variables will include year, type of rotation (e.g., ICU, General Medicine ward, Pulmonary clinic and consult), the year of the resident in training (year 1, year 2, or year 3), the internal medicine residency training site, and for whether the evaluation is from 2 years, or 1 year, prior to implementation of the electronic evaluation system. The electronic evaluations completed in the two years following implementation of the evaluation system will be coded in a similar fashion. However, this data will be able to be exported directly into an Excel or other similar database, minimizing the time required for direct data entry by the data manager. Identities of subjects will also be protected by the same process as above, and by only presenting analyses as group data.

**Progress:** This minimal risk protocol received final approval by the Expedited Review Committee, effective 13 July 2007.

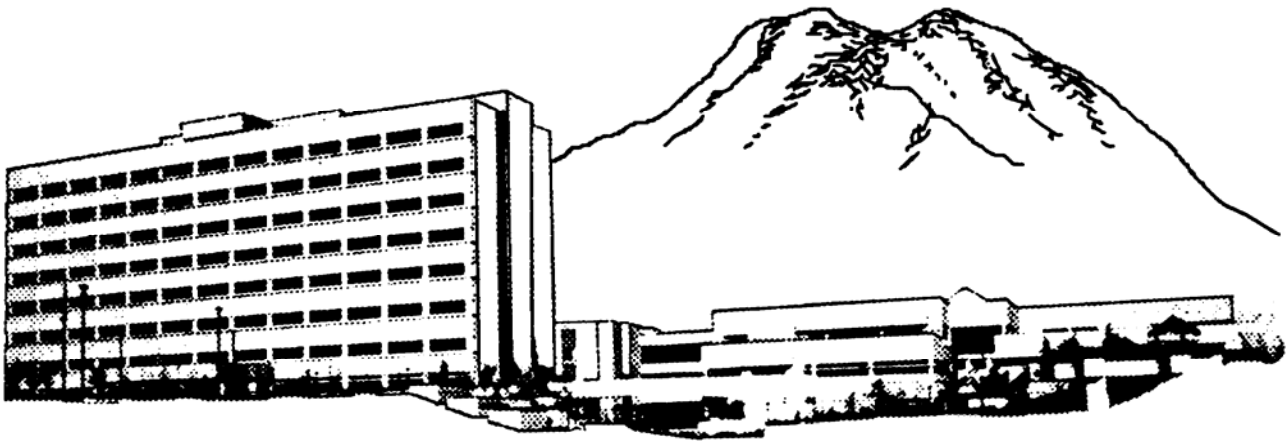
### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207030	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized Placebo Controlled Trial Investigating the Therapeutic Efficacy of Montelukast in the Treatment of Eosinophilic Esophagitis		
<b>Principal Investigator:</b> CPT Mark E. Smith, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Mark D. Cumings, MC; CPT Nathan R. Evans, MC; MAJ Brian P. Mulhall, MC; CPT Michael J. Krier, MC, USAF		
<b>Start - Completion:</b> 2 Mar 2007 - Jun 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 13 Nov 2007

**Study Objective:** The objectives of this study are to prospectively evaluate the therapeutic efficacy (symptomatic and histologic response) of montelukast for the treatment of Eosinophilic Esophagitis (EE), and to further clarify the relationship between EE and gastroesophageal reflux disease.

**Technical Approach:** Up to 30 patients who are followed in the Gastroenterology clinic will be recruited. All patients will then receive a baseline investigation to reveal any associated dysmotility, lower esophageal dysfunction, and/or reflux. Patients will be stratified by GERD and recent esophageal dilation. EGD with proximal, mid, and distal esophagus along with gastric antral and duodenal areas will be biopsied to verify EE only disease. Patients will then be randomized to a six week treatment trial with montelukast or placebo. Patients will then complete a post-treatment symptom score and provide post-trial IgE, CBC, pH/mannometry (GERD group only) and esophageal biopsies to evaluate for treatment effectiveness. Methods of data analysis will include an unpaired T-test and descriptive statistics on demographic data.

**Progress:** This greater than minimal risk protocol was initially approved by the IRB 12 December 2006, and final approval received 2 March 2007. No patients enrolled in FY07 due to a change in the role of PI from Dr. Krier to Dr. Smith, effective in October 2007.



## **Detail Summary Sheets**

Neurology Service, Department of Medicine



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203048	<b>Status:</b> Terminated
<b>Title:</b> A Randomized Trial of B Vitamins for Alzheimer's Disease		
<b>Principal Investigator:</b> LTC Jay C. Erickson, MC		
<b>Department:</b> Medicine/Neurology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Frederick G. Flynn, MC		
<b>Start - Completion:</b> 8 Jun 2004 - Mar 2005	<b>Funding:</b> Upsher-Smith Laboratories via Henry M. Jackson Foundation	<b>Periodic Review:</b> 27 Feb 2007

**Study Objective:** To determine whether B vitamin supplements improve cognitive function in patients with mild-to-moderate Alzheimer's disease.

**Technical Approach:** To test the hypothesis that B vitamin supplements improve cognitive function in patients with Alzheimer's disease, 80 patients with mild-to-moderate Alzheimer's disease will be enrolled in a prospective, randomized, open-label trial. Subjects will be randomized to receive B vitamin supplements consisting of vitamin B12 (0.5 mg qd), vitamin B6 (50 mg qd), and folate (2 mg qd) or no B vitamin supplements over a period of 1 year. Cognitive function, as measured by the Alzheimer's Disease Assessment Scale (ADAS), will be measured at baseline and then after 3 months, 6 months, and 12 months of treatment. The primary outcome will be change in ADAS score compared to baseline. Analysis of variance will be used to test for significant differences between the two treatment groups.

**Progress:** This protocol remains open to enrollment with six subjects enrolled. Five subjects received treatment and four completed study participation. There have been no adverse events reported. Outcome data have not yet been analyzed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203097	<b>Status:</b> Ongoing
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**Title:** CLOSURE I Trial: A Prospective, Multicenter, Randomized, Controlled Trial to Evaluate the Safety and Efficacy of the STARFlex Septal Closure System Versus Best Medical Therapy in Patients with a Stroke and/or Transient Ischemic Attack Due to a Presumed Paradoxical Embolism Through a Patent Foramen Ovale

**Principal Investigator:** LTC Jay C. Erickson, MC

<b>Department:</b> Medicine/Neurology	<b>Facility:</b> MAMC
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**Associate Investigator(s):** COL Beverly R. Scott, MC; COL David T. Schachter, MC; CPT Erek K. Helseth, MC

<b>Start - Completion:</b> 18 Sep 2003 - Oct 2006	<b>Funding:</b> NMT Medical, Inc via Henry M. Jackson Foundation	<b>Periodic Review:</b> 26 Jun 2007
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**Study Objective:** To determine whether the STARFlex Septal Closure System (STARFlex) will safely and effectively prevent recurrent embolic stroke/transient ischemic attack (TIA) and mortality in patients with a patent foramen ovale (PFO) and to demonstrate superiority of the STARFlex device compared to best medical therapy.

**Technical Approach:** The STARFlex Septal Closure System is an investigational device for non-surgical, transcatheter closure of intracardiac defects. The CLOSURE I Trial is a prospective, multicenter, randomized, controlled trial to evaluate the safety and efficacy of the STARFlex System in preventing recurrent cerebrovascular events in patients with a PFO. The study will enroll MAMC patients 18 to 60 years of age who have had a documented stroke or TIA within the last 3 months, have a PFO as detected by transesophageal echocardiography (TEE) with saline contrast bubble study, and do not have any other potentially embolic source or other cause of stroke or TIA. Up to 15 patients will be enrolled at MAMC and a total of 1600 patients will be enrolled at 120 centers in the United States. Investigators will receive training in use of the device. Patients will be randomized to receive implantation of the STARFlex device with concomitant aspirin therapy or medical therapy consisting of aspirin and/or coumadin. Patients who have device implantation will also be treated with clopidogrel (Plavix) 75mg daily for 6 months. All patients will undergo serial physical exams, EKGs, and neurological evaluations (to detect recurrent stroke or TIA) at 6 months, 12 months, and 24 months after device implantation or initiation of medical therapy. Patients who receive the device will also have a transesophageal echocardiogram with saline contrast bubble study and chest x-ray 6 months after implantation to assess for closure of the PFO and condition of the device. The primary endpoints of the study are the 2-year incidence of stroke/TIA and all cause mortality. Data will be analyzed on an intent-to-treat basis using the chi-square test and logistic regression. A central Data and Safety Monitoring Board will inspect and make recommendations regarding rate of stroke/TIA at approximately 10 months and 18 months after start of the study for efficacy or safety concerns.

**Progress:** This protocol remains open to enrollment with nine subjects enrolled. Four subjects received the STARFlex device and five are on the medication arm of the study. One subject has been lost to follow-up, and one moved out of state but continues to be followed there. One patient had a device that failed to open and the device was removed, with no further complications. One patient decided to get another device when randomized to medical therapy, but has agreed to be followed per study's request. Three internal adverse events were reported during FY07, none were assessed as related to study participation. Protocol Version 5.0 and a revised consent form were submitted and approved.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204062	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized Trial of a Migraine Management Seminar in the Treatment of Migraines		
<b>Principal Investigator:</b> LTC Jay C. Erickson, MC		
<b>Department:</b> Medicine/Neurology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Beverly R. Scott, MC; Joan L. Wilson, MSW; CPT Douglas R. Langford, MC		
<b>Start - Completion:</b> 15 Apr 2004 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 13 Mar 2007

**Study Objective:** To determine the effectiveness of a migraine management seminar for improving migraine headaches, migraine-associated disability and migraine-related quality of life.

**Technical Approach:** Subjects will attend a unique, 3-hour, single-session seminar to augment the medical management of migraine headaches. The seminar will educate subjects with migraines about their disorder and various treatments and teach practical non-pharmacologic migraine management skills. The study is a randomized, controlled, single-center trial to determine the efficacy of a migraine management seminar, when used as adjunctive therapy to standard medical therapy in the treatment of migraine headaches. Eighty subjects, fulfilling the International Headache Society criteria for migraines and suffering from significant migraine associated disability will be enrolled in the study. Subjects will be recruited from consecutive subjects referred to the MAMC Neurology Clinic for headache consultation. Study subjects will be randomized to medical therapy (control group) or medical therapy in combination with the migraine management seminar (treatment group). Medical therapy will be determined by each subject's consulting neurologist, will conform to standard of care for the treatment of migraine and not be constrained or otherwise influenced by the study. All subjects will record a standardized headache diary during the study period. The primary outcome measures are number of headache days per month and change in the Migraine Disability Assessment (MIDAS) score. Secondary outcomes include the Migraine Specific Quality of Life (MSQOL) questionnaire score, migraine severity and duration, healthcare utilization and a migraine management satisfaction survey. Outcomes will be assessed at baseline, 3 months after randomization and 6 months after randomization.

**Progress:** This protocol remains open to enrollment with 78 subjects enrolled since April 2004, 26 subjects enrolled in the last reporting period. Sixty subjects have completed study participation and eighteen continue to be actively followed. There have been no adverse events. Data analysis has not yet been initiated. Subject recruitment continues.

### Detail Summary Sheet

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<b>Date:</b> 30 Sep 07	<b>Number:</b> 205115	<b>Status:</b> Ongoing
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**Title:** Study of Acute Viprinex™ for Emergency Stroke: A Randomized, Double-Blind, Placebo-Controlled Study of Viprinex™ (Ancrod Injection) in Subjects Beginning Treatment within 6 Hours of the Onset of Acute, Ischemic Stroke

**Principal Investigator:** LTC Jay C. Erickson, MC

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**Department:** Medicine/Neurology

**Facility:** MAMC

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**Associate Investigator(s):** MAJ Robert B. Blankenship, MC; COL Beverly R. Scott, MC; CPT Jessica D. Lee, MC; MAJ Anna D. Hohler, MC; MAJ Jason A. Friedman, MC; CPT Ere K. Helseth, MC; CPT Douglas R. Langford, MC

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**Start - Completion:**

9 Nov 2005 - Sep 2007

**Funding:**

Neurobiological Technologies, Inc. via Henry  
M. Jackson Foundation

**Periodic Review:**

24 Jul 2007

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**Study Objective:** To determine whether ancrod (Viprinex™) begun intravenously within 6 hours of stroke onset confers statistically benefit in reducing the incidence of disability at 90 days

**Technical Approach:** This is a phase III, double-blind, placebo controlled study to that will be conducted by the Neurology/Stroke Team service at MAMC. Up to 10 subjects may be enrolled; a total of 500 enrolled in the study overall. Eligible subjects will present to the ER with the diagnosis of a stroke and symptom onset within 6 hours before the Ancrod infusion. If patients are eligible to receive rt-PA, they will not be enrolled in this study. Subjects will have a routine history and physical, neurological examination, laboratory tests, a non-contrast CT scan, and a 12 lead ECG. Subjects will be randomized to one of two treatment groups in a biased-coin approach using study-wide balanced enrollment in the two treatment groups by age category (<65, 65-75, >75), independent of stratum assignment. Randomization will be completed via an interactive voice response system. Subjects will receive the 3 hour transfusion and continue to have follow-up after discharge until 90 days after being treated with study medication.

**Progress:** This greater than minimal risk protocol received final approval in November 2005. Since that date, one subject has enrolled and completed the study with an adverse event of a four day hospitalization for near syncope and left sided weakness reported, which was assessed as serious but not unexpected and unrelated to study participation. Amendment #3 was recently submitted and approved. Subject enrollment continues.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205118	<b>Status:</b> Ongoing
<b>Title:</b> Prevalence and Impact of Migraine Among Deployed Soldiers		
<b>Principal Investigator:</b> LTC Jay C. Erickson, MC		
<b>Department:</b> Medicine/Neurology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Brett J. Theeler, MC		
<b>Start - Completion:</b> 5 Aug 2005 - Dec 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 16 Jul 2007

**Study Objective:** (1) To determine the prevalence of migraine among soldiers during military deployment. (2) To determine the frequency and severity of migraine headaches among deployed soldiers. (3) To determine the impact of migraines on soldier readiness during deployment. (4) To determine the diagnosis and treatment patterns of migraine among deployed soldiers.

**Technical Approach:** This is a cross-sectional, observational, questionnaire based study to determine the prevalence, impact, and treatment patterns of migraine among soldiers during military deployment. Approximately 3,000 soldiers of the 1st Stryker Brigade will be asked to voluntarily complete a standardized, validated, headache questionnaire during their post-deployment health evaluation. The questions on the questionnaire are based on the diagnostic criteria of migraine, headache frequency, headache-related disability, and headache treatments. Responses will be used to calculate the prevalence, frequency, severity, and duration of migraines among deployed soldiers. The extent to which migraines impede performance of military duties and current treatment patterns for migraine among this population will also be determined. Dependent variables include: proportion of soldiers experiencing one or more migraine headaches during deployment; mean number of headache days per month; mean duration and severity of headaches; number of missed and sub-optimal duty days attributable to headache; proportion of soldiers with migraine who were previously diagnosed by a healthcare provider and proportion of soldiers with migraine who used migraine-specific medications during deployment.

**Progress:** This protocol has closed patient entry, with 2,725 Soldiers completing study questionnaire. Data continues to be pulled from original questionnaires as well as follow-up questionnaires to further clarify information. Another paper is being prepared for clarification and presentation at this time by associate investigator, Dr. Theeler.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206075	<b>Status:</b> Ongoing
<b>Title:</b> Association Between Migraine and Psychiatric Conditions In Soldiers Returning from Combat		
<b>Principal Investigator:</b> LTC Jay C. Erickson, MC		
<b>Department:</b> Medicine/Neurology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Gregory A. Gahm, MS; Barbara A. Lucenko, PhD; CPT Kristin E. Erickson, MC		
<b>Start - Completion:</b> 4 Apr 2006 - Dec 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8 Mar 2007

**Study Objective:** The objectives of this study are to determine (1) the prevalence of post-traumatic stress disorder (PTSD) among Soldiers with and without migraine headaches (2) the prevalence of depression among Soldiers with and without migraine headaches, (3) the association between PTSD and migraine outcomes in Soldiers, (4) the association between depression and migraine outcomes in Soldiers, (5) the screening prevalence of anxiety among Soldiers with and without migraine, and (6) the association between anxiety and migraine outcomes in Soldiers.

**Technical Approach:** PHQ-9 and PC-PTSD scores will be obtained from the SWAP database for each subject enrolled in the migraine screening database. A single database will be constructed.

**Progress:** This protocol received initial approval on 4 April 2006. Out of the 2,605 subjects screened, 2,167 subjects met inclusion-exclusion criteria. Data analysis is partially complete and remains ongoing. An abstract/poster of study results thus far was presented at a national meeting in May 2007.

**Results:** All health screens were completed by 60% (2167/3621) of soldiers. The screened prevalence was 19% (415/2167) for migraine, 32% (686/2167) for depression, 22% (479/2167) for PTSD, and 13% (271/2167) for anxiety. The prevalence of a positive screen for depression was 50% (206/415) among migraineurs and 27% (480/1752) among non-migraineurs (OR 2.61, p value 0.001). The prevalence of a positive screen for PTSD was 39% (160/415) among migraineurs and 18% (319/1752) among non-migraineurs (OR 2.81, p value 0.001). The prevalence of a positive screen for anxiety was 22% (92/415) among migraineurs and 10% (179/1752) among non-migraineurs (OR 2.50, p value 0.001). The association between co-morbid psychiatric conditions and migraine frequency, duration, and severity will also be presented.

**Conclusions:** After a tour of combat duty in Iraq, soldiers with migraine are more than twice as likely to screen positive for depression, PTSD, or anxiety compared to soldiers without migraine.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207081	<b>Status:</b> Ongoing
<b>Title:</b> An Observational Study of Patients with Headache Disorders Referred for Neurology Specialty Care at a U.S. Army Medical Center		
<b>Principal Investigator:</b> LTC Jay C. Erickson, MC		
<b>Department:</b> Medicine/Neurology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Brett J. Theeler, MC		
<b>Start - Completion:</b> 3 Apr 2007 - Jan 2009	<b>Funding:</b> Comprehensive Neuroscience Program, Uniformed Svcs. University of Health Sciences via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to generate a descriptive database of patients with headache disorders referred to the Neurology Clinic at a U.S. Army Medical Center. The database will be used to examine the demographics, clinical features, causes, triggers, impact, co-morbidities, prescribed treatments, outcomes, and types of headache disorders evaluated by neurologists at a U.S. Army Medical Center during a time of major overseas combat operations.

**Technical Approach:** To facilitate research of headache disorders impacting military members, a headache disorders database will be generated from patient referrals to the neurology clinic at Madigan Army Medical Center. 450 consecutive outpatients diagnosed with headache disorders by the study investigators since January 2006 will be identified using ICD9 codes. Patients with migraine and its variants, post-traumatic headache, medication overuse headache, occipital neuralgia, tension-type headache, cluster headache, other specified headache disorders, or headache disorder not otherwise specified will be enrolled. The baseline neurology clinic note will be abstracted for demographics (age, gender, military status, rank, MOS, past deployments), headache diagnosis, headache frequency (headache days per month), headache severity (0-10 scale), headache duration (hours), headache characteristics (location, nature of pain), headache triggers, migraine disability assessment score (MIDAS), PTSD symptom checklist score (PCL), PHQ-9 depression score, findings on neurologic examination, results of neuro-imaging studies, past treatments, and new therapies prescribed. The presence and severity of traumatic head or neck injury, the cause of traumatic injury, sleep disturbances, post-concussive syndrome, mental health disorders, and analgesic medication overuse will also be recorded. Headache frequency, headache severity, headache duration, and MIDAS scores will be obtained from any follow-up visits that occurred 3-6 months after the initial visit in order to determine changes in these parameters following initiation of treatment. The database will be used to examine the demographics, co-morbid conditions, impact, triggers, outcomes, and types of headache disorders in the study population.

**Progress:** This minimal risk protocol was approved by the Expedited Review Committee on 3 April 2007. As of 23 October 2007, a total of 211 subjects have enrolled in this study at MAMC. Enrollment remains steady each week.

### Detail Summary Sheet

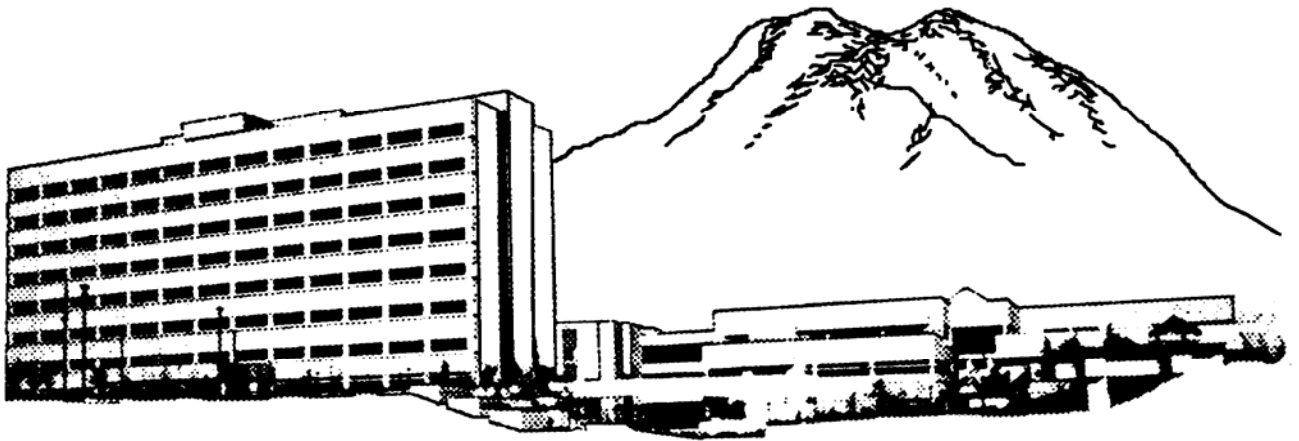
<b>Date:</b> 30 Sep 07	<b>Number:</b> 207104	<b>Status:</b> Ongoing
<b>Title:</b> Sural-Medial Plantar Electrodiagnostic Comparison Study for Tarsal Tunnel Syndrome-Reference Values		
<b>Principal Investigator:</b> MAJ John P. Ney, MC		
<b>Department:</b> Medicine/Neurology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Cdr (Ret) Robert E. Potts, MD		
<b>Start - Completion:</b> 7 Aug 2007 - Jul 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this protocol is to develop a reliable electrodiagnostic technique for the evaluation of tarsal tunnel syndrome.

**Technical Approach:** This study is designed to generate normative values by applying the electrodiagnostic technique to normal, asymptomatic patients. The technique is analogous to the sensitive palmar conduction studies used for evaluation of carpal tunnel syndrome, which tests one nerve likely to be affected in entrapment in the tunnel, and another nerve in the same extremity, which is not anatomically predisposed to compression. Subjects will be examined by one of the investigators, a neurologist, and informed consent will be obtained. Twenty subjects will be tested, with standardized technique and safety precautions.

**Progress:** This greater than minimal risk protocol received initial IRB approval on 26 June 2007, and CIRO concurrence on 17 August 2007.





## **Detail Summary Sheets**

Pulmonary Disease & Critical Care Service,  
Department of Medicine

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206086	<b>Status:</b> Ongoing
<b>Title:</b> Identifying Adherence Obstacles to CPAP Therapy		
<b>Principal Investigator:</b> MAJ Vincent Mysliwiec, MC		
<b>Department:</b> Medicine/Pulmonary & Critical Care		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Robert D. Swanson, PhD; Suzette Gagnon-Bailey, RN; Michael J. Kuculyn; Richard D. Guesford; CPT Brian M. O'Reilly, MC		
<b>Start - Completion:</b> 8 May 2006 - Aug 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 7 May 2007

**Study Objective:** The primary objective of this study is to introduce a survey, in the form of a Concerns Questionnaire that will assess compliance and reasons for non-compliance in patients diagnosed with Obstructive Sleep Apnea (OSA) who are prescribed Continuous positive airway pressure (CPAP).

**Technical Approach:** Subjects with OSA that will be treated with CPAP will be identified by treating provider and scheduled for follow up within 3 months. Subjects will return for follow up with the downloaded data from CPAP machine and compliance data downloaded. During this time patients will complete the "PAP Concerns Questionnaire." The downloaded data are transferred to "CPAP Concerns Questionnaire" for analysis.

**Progress:** This protocol remains ongoing, with 120 subjects participating thus far. An amendment was submitted with a rewritten/new questionnaire that will be completed by new patients utilizing CPAP. Subject accrual will continue until 300 questionnaires have been completed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205128	<b>Status:</b> Ongoing
<b>Title:</b> Impulse Oscillometry and Obstructive Lung Disease: Assessment of a Clinically Significant Bronchodilator Response		
<b>Principal Investigator:</b> LTC Alexander S. Niven, MC		
<b>Department:</b> Medicine/Pulmonary & Critical Care		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Suzette Gagnon-Bailey, RN; LTC Cynthia L. Clagett, MC; MAJ John P. Rinard, MC; CPT Johathan R. Coyle, MC; MAJ William F. Kelly, MC; MAJ Vincent Mysliwiec, MC; MAJ Steven P. Bennett, MC; CPT Charles C. Broy, MC		
<b>Start - Completion:</b> 14 Dec 2005 - Sep 2008	<b>Funding:</b> Amarillo Pulmonary via MAMC	<b>Periodic Review:</b> 28 Aug 2007

**Study Objective:** This study will (1) evaluate asymptomatic nonsmokers using impulse oscillometry (IOS) and conventional pulmonary function tests before and after bronchodilator administration to determine the normal adult bronchodilator IOS responses to albuterol and (2) evaluate the ability and extent to which IOS can identify airway changes in asymptomatic smokers, patients with asthma and chronic obstructive lung disease (COPD) compared to standard pulmonary function testing.

**Technical Approach:** 89 asymptomatic nonsmoker volunteers will be recruited from the hospital staff. 89 asymptomatic smokers will be recruited from the hospital staff and family members of patients visiting Madigan AMC for medical appointments. Based on prior literature suggesting that 50% of asthmatics and 10-15% of COPD patients will have evidence of reversible airway obstruction, 178 asthmatics and 890 patients with COPD will need to be enrolled to examine this important variable. These subjects will be recruited from routine outpatient referrals to the Pulmonary Function Lab for clinical testing.

All asymptomatic subjects will complete a questionnaire on their demographics, medical and smoking history, and a review of systems to confirm the absence of cardiopulmonary complaints. Height, sitting height, and weight will be measured in each subject. Four IOS measurements of 60-90 seconds each will be performed followed by standard spirometry and lung volume measurements. Each subject will receive 3 inhalations of albuterol 90 micrograms using a spacer device and repeat the IOS, spirometry, and lung volume measurements after 10 minutes. Subjects with asthma and COPD will undergo the same protocol, with the addition of completing a validated asthma or COPD questionnaire to evaluate the severity and impact of their respiratory disease on their daily activities.

The primary outcome variables for IOS will include the respiratory impedance ( $Z_{rs}$ ), respiratory resistance at 5, 15, and 20 Hz ( $R_5$ ,  $R_{15}$ ,  $R_{20}$ ), frequency dependence from 5-15 Hz and 5-20 Hz ( $R_{5-15}$ ,  $R_{5-20}$ ), the respiratory reactance at 5 Hz ( $X_5$ ) and the reactance area (AX), the resonant frequency ( $f_{rs}$ ) before and after bronchodilator administration. The primary outcome variables for conventional pulmonary function testing will be the forced vital capacity (FVC), the forced expiratory volume in 1 second (FEV1) and 6 seconds (FEV6), the ratio of FEV1 to FVC, body plethysmography measurements for functional residual capacity (FRC), inspiratory capacity (IC), and vital capacity (VC) before and after bronchodilator administration. Summary statistics, frequency and/or contingency tables will be provided for all variables of the study. Baseline and post-bronchodilator IOS variables will be correlated to conventional pulmonary function measurements using a paired t test. The impact of variables age, height, sitting height, race, gender, and allergy symptoms will be evaluated using the Analysis of Variance (ANOVA) and the Multivariate Analysis of Variance (MANOVA). Comparison between measurements obtained in asymptomatic nonsmokers and measurements obtained in asymptomatic smokers, asthmatics and COPD subjects will be performed using ANOVA. Pearson's R correlations between IOS

measurements, conventional pulmonary function measurements, and questionnaire based symptom scores will be obtained and the impact of the variables listed above will also be evaluated.

**Progress:** A total of 15 patients have been enrolled over the last 12 months. Recruitment during FY07 has been slow due to staff shortages in the PFT lab and the deployment of the PI. A significant number of asymptomatic nonsmokers and a small number of asymptomatic smokers have been enrolled. An increase in enrollment is anticipated in the upcoming year.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207093	<b>Status:</b> Ongoing
<b>Title:</b> Effect of Dried Garlic Supplements on Pulmonary Gas Exchange: A Prospective, Double Blinded, Crossover, Pilot Study		
<b>Principal Investigator:</b> LTC Alexander S. Niven, MC		
<b>Department:</b> Medicine/Pulmonary & Critical Care		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Michael J. Loughren, AN, CRNA; Danny D. Shen, PhD; Katherine A. Simonson, RN		
<b>Start - Completion:</b> 18 Jul 2007 - Apr 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to determine if treatment with a dried garlic powder supplement improves pulmonary gas exchange in healthy adults.

**Technical Approach:** In this pilot study, eight healthy men and women age 18 to 50 will be enrolled. After a two week course of garlic supplement or placebo, subject's pulmonary gas exchange will be analyzed using indirect calorimetry. Following a two week washout period subjects will "crossover" and repeat the two week course of dried garlic or placebo and gas exchange testing. A number of respiratory parameters will be collected to determine the participant's ventilatory equivalent for oxygen, ventilatory equivalent for carbon dioxide, alveolar - arterial difference for PO<sub>2</sub>, and ratio of physiologic dead space to tidal volume. These variables will allow an assessment of the effectiveness of ventilation and the degree of ventilation- perfusion mismatching. Investigators believe dried garlic powder supplement will improve ventilation and decrease ventilation- perfusion mismatching. Variables will be compared by T-tests.

**Progress:** This greater than minimal risk protocol received initial IRB approval 22 May 2007, and final approval on 18 July 2007. A protocol amendment adding Katherine Simonson, RN, as associate investigator was approved 23 October 2007. Enrollment remains pending delivery of garlic supplements.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 207094	<b>Status:</b> Ongoing
<b>Title:</b> A 26-week treatment, multicenter, randomized, double-Blind, double-Dummy, placebo-controlled, adaptive, seamless, parallel-group study to assess the efficacy, safety and tolerability of two doses of indacaterol (selected from 75, 150, 300, & 600 mcg o.d.) in patients with chronic obstructive pulmonary disease using blinded formoterol (12 mcg b.i.d.) and open label tiotropium (18 mcg o.d.) as active controls			
<b>Principal Investigator:</b> LTC Alexander S. Niven, MC			
<b>Department:</b> Medicine/Pulmonary & Critical Care			<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Linda L. Brown, MC			
<b>Start - Completion:</b> 16 Aug 2007 - Jul 2008		<b>Funding:</b> Novartis via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A
<b>Study Objective:</b> Primary objective is to demonstrate superiority of at least one dose of indacaterol (selected at study Stage I from 75, 150, 300, or 600 mcg o.d. via single dose dry powder inhaler, SDDPI) versus placebo with respect to 24 hour post dose (trough) FEV1 after 12 weeks of treatment in patients with COPD.			
Secondary Key: to demonstrate non-inferiority of at least one dose of indacaterol (selected at Stage I from 75, 150, 300 or 600 mcg o.d. via SSDPI) versus open label Tiotropium (18 mcg od) with respect to 24 hour dose (trough) FEV1 following 12 weeks of treatment. Important: to evaluate the effect of two doses of indacaterol (selected at Stage I from 75, 150, 300 or 600 mcg o.d. via SSDPI) on the percentage of "days of poor control" reported over the 26 week randomized treatment period, as compared to placebo. Other objectives listed in detail in the master protocol amendment I page 5 and original protocol pages 16-17			
<b>Technical Approach:</b> This is a multi-center, double-blind, double dummy, placebo-controlled, adaptive, seamless (sponsor designed phrasing which means this is a dose evaluation and efficacy protocol combined) parallel group design with blinded formoterol and open label tiotropium as active controls. The study consists of two stages with the overall aim of obtaining pivotal confirmation of efficacy, safety and tolerability after 26 weeks of treatment with indacaterol in patients with COPD. The first stage of the protocol is designed to study dosing efficacy; however, that phase will probably be completed before MAMC is ready to begin subject recruitment and enrollment. Enrollment at MAMC is anticipated to begin with the efficacy Stage 2 of the protocol.			
Stage 1 (dose selection) patients will be randomized to one of seven treatment groups (indacaterol 75, 150, 300, 600 mg, formoterol, placebo, or open label tiotropium) in a 1:1:1:1:1:1:1 ratio. The indacaterol and formoterol doses will be given in a double-blind double dummy design. An interim analysis will be performed when 115 patients in each of the seven treatment groups have been randomized (at least 805 patients in total). Allowing recruitment to all treatment groups will be suspended when the 115 patients per treatment arm needed for Stage 1 have been randomised.			
Stage 2, recruitment of patients to four treatment groups (the two chosen indacaterol doses from Stage 1, placebo and tiotropium) will recommence in a 1:1:1:1 randomization ratio to obtain pivotal confirmation of efficacy and safety data of indacaterol for 26 weeks of treatment. Patients in both stages will follow the same visit schedule.			
<b>Progress:</b> This greater than minimal risk protocol received initial IRB approval 22 May 2007, and final approval on 16 August 2007. Protocol documents were released to the study staff following CRADA/SOW approval 10 September 2007.			

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207099	<b>Status:</b> Ongoing
<b>Title:</b> Evaluation of the Number and Variety of Procedures Done by Army General Internists: A Survey		
<b>Principal Investigator:</b> LTC Alexander S. Niven, MC		
<b>Department:</b> Medicine/Pulmonary & Critical Care		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ John P. Rinard, MC; LTC Cecily K. Peterson, MC; COL Bernard J. Roth, MC		
<b>Start - Completion:</b> 5 Jun 2007 - Sep 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

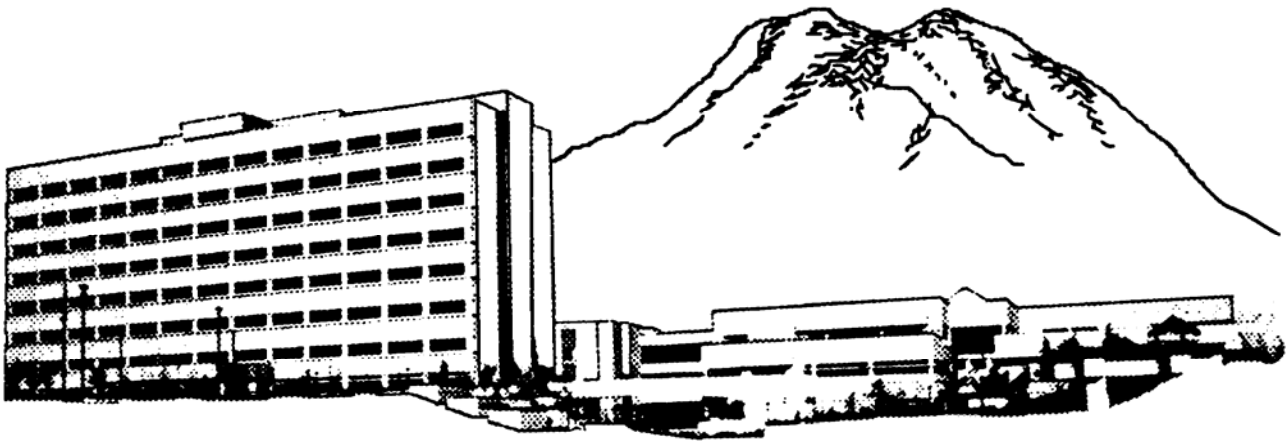
**Study Objective:** To evaluate the variety and volume of procedures performed by Army general internists in their daily practice and during deployment.

**Technical Approach:** Using the Outlook Global AQQQ, an email survey will be sent to the current roster of active duty Army 61F physicians by Ms Borsic, in June 2007. Surveys returned to Ms Borsic will have their data entered into an Excel data spreadsheet with a sequential numerical identifier assigned for each respondent to ensure anonymity. Ms Borsic will then e-mail remaining non-respondents two additional times with the second e-mail in July and August 2007 to maximize response rate. Returned surveys during these repeat contacts will be recorded in the same manner.

The survey used for the study recently performed by Wigton et al. was obtained with the primary and second authors' consent, and modified in the following ways: (1) "or 20\_\_" was added to medical school graduation date due to consideration of the large population of young staff general internists currently in practice in the Army. (2) The question on the practice site was modified to reflect locations of Army general medicine practice instead of city size. The question on the number of beds in the physician's primary hospital was changed to the name and location of the hospital in which the respondent practices. As we know the locations of our Army facilities, we will be able to more accurately identify the number of beds and surrounding population of these medical facilities without introducing bias from our respondents. (3) The question in the original survey on the amount of income that was based on clinical productivity was replaced with two questions related to deployment. (4) The question asking respondents if they would be willing to be contacted with further questions was added. (5) The list of procedures was modified to include chest tube placement, repair of lacerations, cardiac arrest / code, and others to better reflect common additional procedures that may be encountered in military general medicine practice.

Percutaneous liver biopsy was deleted due to space issues and the perceived low prevalence of this procedure among Army general internists. (6) The "while deployed" column was added to allow differential assessment of procedures performed at home and during deployment. The database, roster, and numerical identifier list with assigned names will be maintained and secured by Ms Borsic in her office.

**Progress:** A total of 35 patients have been enrolled in this study during FY07. The study survey was originally circulated in early September, due to logistical issues coordinating survey distribution and to allow individuals leaving the area to arrive at their new duty station to maximize study participation. A second reminder e-mail will be sent after Army ACP, with ongoing continued data collection.



# **Detail Summary Sheets**

## **Nutrition Care Division**



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207091	<b>Status:</b> Ongoing
<b>Title:</b> A Comparison of the Futrex-6100/XL Body Composition Analyzer and Dual Energy X-Ray Absorptiometry (DEXA) for Accuracy and Reliability of Percent Body Fat Measurement		
<b>Principal Investigator:</b> LTC Karen L. Geisler, SP		
<b>Department:</b> Nutrition Care		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Mary S. McCarthy, PhD; 1LT Kyle Peper, SP		
<b>Start - Completion:</b> 25 Jun 2007 - Jul 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this descriptive study is to compare results obtained for body fat mass/percent body fat in adult patients undergoing dual-energy x-ray absorptiometry (DEXA) with the results obtained from a portable, hand-held Futrex-6100/XL body composition analyzer.

**Technical Approach:** The is a cross-sectional descriptive study to compare results obtained for percentage of body fat in adult patients undergoing dual-energy x-ray absorptiometry (DEXA) evaluation with the results obtained from a portable, hand-held Futrex-6100/XL body composition analyzer. The technical assistant, Ms. Jeannie Chevalier who is the DEXA scanner technician will assist the team by alerting team members to dates and times that adults are scheduled for routine DXA scans over the next year. One of the team members (Geisler, McCarthy, or Peper) will go to Nuclear Medicine and approach patients waiting for their scan to ask them if they would consider enrolling in our study to compare percent body fat results between their DEXA scan and our Futrex-6100/XL body composition analyzer. The following data will be collected for this study: height, weight, and percent body fat (measured by DEXA full body scan and Futrex scan). Standard of care for a DEXA scan is measurement at two sites (spine and pelvis). The team member recruiting the patient will go over the informed consent document and answer any questions. If they decide to proceed with the study, the researcher will obtain signed informed consent, current height and weight measurements followed by a full body DEXA scan and Futrex scan. This procedure will take approximately twenty minutes. The patient will be told the results of the Futrex scan but results from the DEXA scan may not be immediately available. The patient will be allowed to leave following the Futrex scan. All study data will be entered into a spreadsheet on a computer in the PI's office.

**Progress:** This minimal risk protocol received initial IRB approval 22 May 2007, and final approval on 25 June 2007. No subjects enrolled during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206008	<b>Status:</b> Completed
<b>Title:</b> Attenuation of Exertional Muscle Damage with a Nutritional Supplement		
<b>Principal Investigator:</b> CPT Michael J. Hartenstine, MS		
<b>Department:</b> Nutrition Care	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Colleen Cates-Gorang, R.D., CDE; LTC Leslee F. Sanders, MC; Patricia A. Deuster, PhD; MAJ Steven D. Mahlen, MS; CPT Eric Grenier, SP		
<b>Start - Completion:</b> 9 Feb 2006 - Aug 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 26 Sep 2006

**Study Objective:** Determine the extent to which ingestion of a carbohydrate (CHO)-electrolyte beverage with essential amino acids (EAA) to include glutamine, by soldiers during and after strenuous exercise prevents exertional muscle damage (EMD) as compared to a carbohydrate-electrolyte beverage alone. Biochemical analysis will include measuring plasma markers of damage such as creatine kinase (CK) and interleukin-6 (IL-6), blood in urine and subjective measurements of pain in a group of soldiers before, after, and 48 hours after a strenuous military training event.

**Technical Approach:** The study will be a randomized, double-blind, crossover design utilizing Fort Lewis soldiers as the study population. Subjects will be divided into two groups of a minimum of ten per group and assigned to one of two treatment conditions, either receiving a placebo beverage or the treatment beverage. Both beverages will be manufactured by the Gookinaid Company per the following specifications: the placebo beverage will contain 45-60 grams of carbohydrate per liter, 270 milligrams of sodium and 400-500 milligrams of potassium providing a calorie range of 180-240 per liter (similar to a commonly available sports drink such as Poweraid); the treatment beverage will consist of the placebo plus 5 grams per liter of essential amino acids and 3.5 grams per liter of glutamine and provide 215-275 calories per liter (equivalent to adding a glutamine powder such as ProLab Glutamine® to a sports beverage or utilizing a sports beverage such as Growling Dog Replacement Drink®, both widely available for purchase).

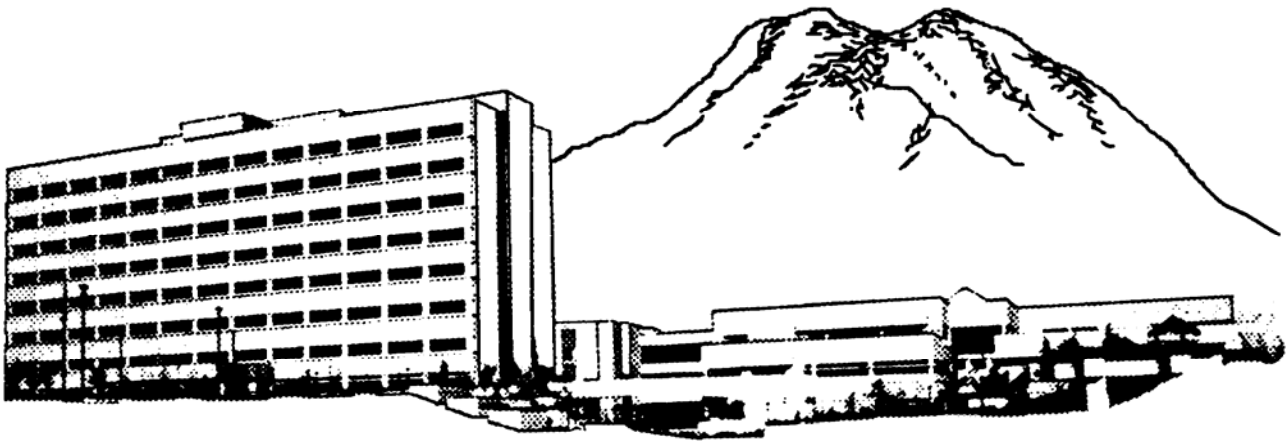
The subjects will participate in a 7 ½ mile road march carrying a backpack weighted to 30% of his/her body weight (up to a maximum of 83 pounds) - or an event similar in difficulty level. A minimum of 1 liter of beverage will be ingested each hour during the event and an additional 1 liter of beverage consumed within two hours afterwards. After a 7-14 day washout period, the event will be repeated, with the subjects consuming the alternate beverage; each subject is acting as his/her own control to determine difference in treatment effect. Within subject and between treatment group comparisons will be performed using ANOVA. Performance, metabolic and muscle damage response data will be evaluated with repeated-measures ANOVAs and t-tests. Dietary intake of specific nutrients will be estimated for each subject using the 4-day food record, (previously validated and utilized at the University of Washington) and analyzed with software from the University of Minnesota - Nutrient Data System for Research (or similar software).

**Progress:** This protocol was reported as completed in June 2007, with 36 Soldiers completing both phases of study.

**Results:** There were no significant differences ( $p > 0.05$ ) between beverages with respect to changes in biomarkers of muscle damage or inflammation, as measured at baseline and after exercise with respect to changes in creatine kinase, lactate dehydrogenase, white blood cell counts, and select pro- and anti-inflammatory cytokines. Plasma glutamine levels remained relatively unchanged between placebo and treatment conditions, with both beverages blunting post-exercise induced decreases. Findings of interest, though not reaching statistical significance, include slightly greater elevations of CRP, TNF- $\alpha$  and pain scores with treatment following exercise,

implying that the additional glutamine may actually enhance the inflammatory response. There was a trend in improved performance as measured by number of stairs-stepped after exercise, treatment compared to placebo ( $p = 0.13$ ).

Conclusion: Our findings suggest that the addition of glutamine to a CHO/EAA beverage provided during exercise doesn't provide significant additional benefit over a CHO/EAA beverage alone in attenuating EMD or improving physical performance. These preliminary findings imply glutamine may enhance the inflammatory response, which may allow cells to better combat tissue damage. The trend in improved physical performance suggests that glutamine may also affect some aspect of protein synthesis during exercise or recovery, thus allowing subjects to better perform physical tasks.



# Detail Summary Sheets

Department of Nursing

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206093	<b>Status:</b> Ongoing
<b>Title:</b> Effects on Aspirated Volume, Patency, and Tracheal Mucosa using High Intermittent Negative Pressure versus Low Continuous Negative Pressure for Subglottic Secretion Aspiration		
<b>Principal Investigator:</b> LTC Tina A. Connally, AN		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Cynthia L. Clagett, MC; MAJ Steven P. Bennett, MC; Mary S. McCarthy, PhD; Nora A. Regan, CRT; MAJ William F. Kelly, MC; LTC Alexander S. Niven, MC; MAJ Jeffrey B Musser, MC; Charlotte L. DePew, RN, MSN		
<b>Start - Completion:</b> 1 Aug 2006 - Dec 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 22 May 2007

**Study Objective:** Objectives: To determine the effect on aspirated secretion volume using high intermittent versus low continuous subglottic secretion aspiration with the HiLo Evac endotracheal tube. To determine the effect on line patency using high intermittent versus low continuous subglottic secretion aspiration with the HiLo Evac endotracheal tube. To describe the effect on tracheal mucosa using photographic images obtained endoscopically when evaluating high intermittent versus low continuous subglottic secretion aspiration with the HiLo Evac endotracheal tube.

**Technical Approach:** This study will use a prospective, quasi-experimental design to answer the important questions about maintaining line patency, effectively removing secretions, and minimizing mucosal trauma from applied negative pressure. Sixty subjects will be required with 30 per group receiving either low continuous suction or high intermittent suction. Method of suction will alternate each month for 6 months. Patients will be included if they require mechanical ventilation for longer than 3 days. At that point consented patients will receive a baseline video-assisted tracheoscopy at the time of their routine subglottic suctioning intervention. Mucosal trauma will be graded according to the Modified Mathias-Wedley Tool. From that point on, patients will receive a once daily video-assisted tracheoscopy every one to three days with grading of any mucosal injury. A secretion specimen taken during the tracheoscopy from above the cuff will be submitted for microbiologic examination. Patency and secretion volume aspirated will also be recorded daily. Data will be analyzed by Student's t test for group comparisons and ANOVA/ANCOVA for individual / group comparisons over time. The results will be used to finalize the evidence-based practice protocol for prevention of VAP in the MAMC ICU.

**Progress:** Approved protocol documents were released to the study staff 1 August 2006. Consenting ample subjects has proven more difficult than initially projected. Complete data sets have been obtained on 3 out of the 8 subjects entered into the study for two reasons; intubation less than 72 hours and specimen not saved by nursing staff as required. Investigators missed 12 opportunities to enter subjects due to lack of staff physician support to perform the initial tracheoscopy, failure to identify subjects that qualify (especially after normal business hours), misconception about inclusion criteria, initial lack of a surrogate consent form, and then 3 surrogates that did not want to give consent. To combat these issues, an in-service has been conducted and information signs posted for MAMC staff. It also took 6 months for Anesthesia to use only the Hi-Lo Evac tube in the emergency bags, which probably prevented the enrollment of an additional 10 subjects as all emergent intubations were done with a regular ETT. With this problem resolved, study staff continues to identify obstacles, intervene, and monitor for further obstacles in order to reach the intended enrollment goal of 60 evaluable subjects.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207101	<b>Status:</b> Completed
<b>Title:</b> A Retrospective, Exploratory Study Evaluating Incidence of Postoperative Urinary Retention (POUR) and Its Effect on Post-Anesthesia Care Unit (PACU) Discharge		
<b>Principal Investigator:</b> W. Terry Feliciano, RN		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Eulalia J. Montero, RN; CPT Melissa D. Priester, MD, MC; Mary S. McCarthy, PhD		
<b>Start - Completion:</b> 12 Jun 2007 - Dec 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objectives are to describe the incidence of postoperative urinary retention (POUR) in the Post-Anesthesia Care Unit (PACU) setting in our facility, determine if the incidence of POUR impacts the length of stay in the PACU, and identify characteristics of patients who are at risk for POUR in order to justify development of a protocol for management of POUR.

**Technical Approach:** The research team will jointly review the PACU admission database for patients that have been previously identified as experiencing postoperative urinary retention between 1 June 2005 and 31 May 2007. For patients that have been diagnosed with POUR the following variables will be collected: age, gender, type (service & location) and duration of surgery, type of anesthesia, amount of intraoperative fluids, bladder volume on entry to the PACU, bladder volume subsequently drained with one-time catheterization /indwelling catheter placement, time to void, and time to discharge. Data will then be collected from an equal number of patients without the diagnosis of POUR. Using these data, statistical analyses will be performed to describe the incidence of POUR, to help identify predictive factors of POUR, and to determine if the intervention of a one-time catheterization led to decreased length of stay with earlier discharge home from the PACU.

**Progress:** This minimal risk protocol received final approval by the Expedited Review Committee, effective 12 June 2007. No progress has been reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207086	<b>Status:</b> Ongoing
<b>Title:</b> A Prospective, Randomized Study of the Effectiveness of Aromatherapy for Relief of Postoperative Nausea & Vomiting		
<b>Principal Investigator:</b> Nancy S. Hodge, RN, MSN		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Catherine D. Sumner, RN; Mary S. McCarthy, PhD; MAJ Laura L. Feider, AN		
<b>Start - Completion:</b> 6 Jul 2007 - Apr 2008	<b>Funding:</b> Soothing Scents, Inc via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this prospective, randomized, pre-test-post-test study is to compare the effectiveness of two types of aromatherapy (Quease-Ease versus Isopropyl alcohol) in relieving postoperative nausea and vomiting (PONV).

**Technical Approach:** This study will compare the effectiveness of two types of aromatherapy on relief of PONV. The experimental group will use a Quease-Ease inhaler while the control group will use a standard aromatherapy option offered to postoperative patients, vapor inhalation of isopropyl alcohol. It is anticipated that about one hundred and forty postoperative patients will be enrolled over twelve months with randomization to two equal groups. Patients will be consented during preoperative work up and will enroll in the study upon the first episode of nausea on the postoperative unit. Patients will rate nausea in a pre-test, post-test manner on a 10-point Likert-type scale, before and after receiving the aromatherapy intervention. At 24 hours or upon discharge, whichever comes first, the patient will be asked to rate their satisfaction with overall management of nausea and their perceived effectiveness of the aromatherapy treatment. Demographic data will be collected from the medical record. Ten percent of patients, about seven patients from each group, will be asked to volunteer for an interview that asks more in-depth questions about the experience of PONV and the use of aromatherapy. Data analysis will be performed using unpaired t tests to compare changes in nausea score, and to compare patient satisfaction and perceived effectiveness of aromatherapy scores.

**Progress:** This minimal risk protocol was initially approved by the IRB on 24 April 2007, and final approval received on 6 July 2007. Protocol documents were released to the study staff on 6 November 2007, following resolution of funding issues for this protocol.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207076	<b>Status:</b> Completed
<b>Title:</b> Evaluation of the Sexual Awareness Kit (SAK)		
<b>Principal Investigator:</b> LTC Denise Hopkins-Chadwick, AN		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Victoria von Sadovszky, USAF; LTC Nancy Ryan-Wenger, MC		
<b>Start - Completion:</b> 14 Mar 2007 - Mar 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to evaluate a prototype of a self-administered safer sex intervention specifically designed for military women.

**Technical Approach:** This is a descriptive study to collect qualitative data on women's evaluation of a self-administered safer sex intervention (SAK) specifically designed for women who travel to austere environments (i.e., military women). The sample population will be women age 18-55 years who are currently serving in the Army or Army Reserve and are either deployable or have been deployed in the past. Focus groups or interviews totaling 10 women will be used to determine the women's perceptions about the acceptability and feasibility of the SAK through the use of a structured interview schedule developed by the investigators. Descriptive statistics will be used to describe the participants, and their representativeness of women in the Army. The open-ended interview responses will be analyzed using McLaughlin and Marascuilo's content analysis method. Findings will be reported according to the items in the interview schedule.

**Progress:** This minimal risk protocol was approved by the Expedited Review Committee on 14 March 2007. Ten subjects participated at MAMC in this a multi-center study; data will be analyzed by associate investigators at Ohio State University. No further work on this phase of the protocol will be conducted at MAMC, and the study was reported as completed on 9 August 2007. No abstract is available at this time.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 201104	<b>Status:</b> Ongoing
<b>Title:</b> Newborn Infant Speech Perception		
<b>Principal Investigator:</b> Lori A. Loan, RNC, PhD		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Randall C. Zernzach, MC, USAF; Tricia K. Grannis, R.N.; Christine Moon, PhD		
<b>Start - Completion:</b> 13 Jun 2001 - May 2003	<b>Funding:</b> UW	<b>Periodic Review:</b> 29 May 2007

**Study Objective:** Characterize the effect of experience on typically developing newborn infants' perception of speech and language.

**Technical Approach:** The current proposal for research is for a 2-year study of newborn infant discrimination of familiar and unfamiliar speech sounds. Three experiments will comprise the study. The first will test newborns' ability to discriminate mother's voice from a stranger voice when the speech samples are brief. The second experiment will examine whether infants respond preferentially to their mother's native language when the samples are brief. In the third experiment, infants will be tested for their ability to discriminate brief vowel sounds from among well- and poorly-formed exemplars in English. Each of the three experiments will require data from 80 participants for a total of 240 infants. Because the attrition rate for completion of the 10-minute session is likely to be about 35%, it is expected that approximately 360 infants will be recruited and that 120 will not complete the experiment.

Prospective participants will be 1-5 days old and will be identified from hospital records. Eligibility will be based upon criteria that indicate typical, uncomplicated newborn development. Parents will be contacted in their hospital rooms by the experimenters who will present the study and obtain signed, informed consent. Infants will be transported to a quiet area near the newborn unit for a 20-minute session. A pacifier that is connected to a pressure transducer will be placed in the infant's mouth. If the pacifier is accepted, headphones will be placed over the infant's ears. After a 1-minute baseline period to measure sucking pressure, computer-controlled sounds at conversational levels of intensity will be presented for 9 minutes, contingent upon infant sucking pressure. Frequency of sucks during particular stimuli will be the dependent measure. Data analysis will be based upon a comparison of sucking frequency during different sounds. Results of the experiments will be presented at professional conferences and submitted as articles for publication in professional journals.

**Progress:** Data collection and preliminary analyses continued during FY07. Due to an unexpected loss of research funding during FY06, the pace of data collection slowed during the past year; however, analysis of data in the database continued. The analyses confirm newborn recognition and preference for mother's voice, and they extend past results by demonstrating that pitch of the voice (fundamental frequency and/or spectral slope) is an important cue to voice recognition by newborn infants. This is consistent with the idea that newborns are relying on prenatal voice cues for postnatal perception. Pending replication of the pitch results, a paper on the topic will be submitted to an infant development journal.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 202066	<b>Status:</b> Completed
<b>Title:</b> Caring Interventions for Couples Who Have Miscarried		
<b>Principal Investigator:</b> Lori A. Loan, RNC, PhD		
<b>Department:</b> Nursing		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Kristen M. Swanson, RN, Ph.D., FAAN; Mark A Biernbaum, Ph.D.; Kathryn Barnard, RN, Ph.D., FAAN; Martha J. Lentz, BSN, MN, Ph.D.; Margaret M. Heitkemper, Ph.D.		
<b>Start - Completion:</b> 16 May 2002 - Oct 2004	<b>Funding:</b> NIH via MIPR	<b>Periodic Review:</b> 9 May 2006

**Study Objective:** The purpose of this randomized study is to compare the effects of nurse caring (3 nurse counseling sessions), self-caring (3 home-delivered video tapes and journals), combined caring (1 nurse counseling session plus 3 videotapes and journals) and no intervention (control) on the emotional healing, integration of loss and couple well-being of women and their partners (husbands or male mates) in the first year after miscarrying.

**Technical Approach:** 340 couples(or 680 individuals) will be recruited to participate in a 4 group, pre-test, post-test randomized study of a counseling intervention meant to reduce distress and enhance couple well-being following miscarriage. Upon recruitment, individuals will be informed that they may be randomized into a group that will not receive any treatment. Four groups will be followed for 1 year. All participants will fill out 4 questionnaire packets throughout the study period. The first will be mailed after the couple initially agrees to participate. The other questionnaire booklets will be sent at 6 weeks, 16 weeks and 1 year after their initial enrollment in the study.

**Progress:** This study completed all recruitment and all participants have completed the interventions. Twelve MAMC couples who were referred to the UW study team chose enrolled. MAMC's role in the study consisted of handing out study brochures to potentially eligible couples. No brochures were handed out this year as the study recruitment phase was done. The protocol was reported completed at MAMC in September 2007. Data analysis is nearly complete, and the study will remain open at the UW IRB until all publications are completed; at least 2 more years.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 202075	<b>Status:</b> Ongoing
<b>Title:</b> Secondary Analysis of NICU Modified Care Environment Projects		
<b>Principal Investigator:</b> Lori A. Loan, RNC, PhD		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Karen A. Thomas, Ph.D., RN; Susan T. Blackburn, Ph.D., RN, FAAN; Shu-Yuann Wang, MS, RN; Sara Brown, RN; Shao-Yu Tsai		
<b>Start - Completion:</b> 10 Jun 2002 - May 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8 May 2007

**Study Objective:** Secondary analysis of data collected in previously approved projects is proposed. Prior human use approvals were (1) The Effects of a Modified Care Environment on the Growth and Development of High Risk Infants, P.I. LTC Michelle T. Renaud, approved 4 September 1992, and (2) a continuation and extension, Neonatal Outcomes in a Modified NICU Environment, P.I. LTC Michelle T. Renaud, approved 13 July 1993. Additionally these projects were approved by the University Of Washington Human Subjects Division. Both projects included Karen Thomas and Susan Blackburn, UW faculty, as Co-Principal Investigators.

The original projects involved comparison of two neonatal intensive care unit environments that included reduced light and sound levels. Infants randomized to the control group remained in the standard nursery. Both groups of infants received standard medical and nursing care in all respects, except for the nursery environment. Data collect during the study included infant health status, parent demographic information, duration of hospitalization, environmental sound and light levels, neurologic and behavioral assessment and infant sleep-wake states. Infant sleep-wake stated was measured by 3-4 hour video recordings performed at 34 weeks gestational age and again at time of discharge. Video recordings were performed while infants were in incubators or in open crib and display the infant's body and face.

For the second analysis, investigators are requesting permission for activities: (1) Photo copies to be made of existing video coding sheets, (2) Access to video tapes for recording purposes, (3) Use of existing data base by the three graduates named above.

**Technical Approach:** The proposed research is a secondary analysis of data from a previously approved project that was conducted at MAMC in conjunction with nurse researchers from the University of Washington Department of Family and Child Nursing. Permission is requested for use of data by a total of three nursing graduate students. Computer files containing the data from the original project, excluding identifiers, is currently in the possession of Karen Thomas. Permission is requested to photocopy the video coding sheets, currently held at MAMC for use by investigators at the University of Washington. Permission is also requested for temporary use of the videotapes at the U.W. The video coding sheets will be used to enter the raw data into a computer file. Videos will be used to determine reliability of original coding and to code additional infant behaviors and care giving activities.

**Progress:** During FY07, one doctoral student, Shu-Yuann Wang, continues to analyze data from the parent project. This data is anonymized; investigators at the University of Washington do not have access to the original code list, and the data set does not include any information which would allow identification of subjects. Ms. Wang will complete her dissertation by June 2006. Two graduates, Shao-Yu Tsai and Sara Brown, whose Masters theses were based on the secondary analysis, along with Dr. Karen Thomas, have submitted a journal manuscript based on study findings. Ms. Tsai's poster presentation at the Western Institute for Nursing conference (An Exploratory Analysis: Environmental Modifications on the Sleep-Wake State in Preterm Infants - Portland, OR, 2004) received an award for doctoral student research.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 204031	<b>Status:</b> Ongoing
<b>Title:</b> Military Nursing Outcomes Database: Analysis & Expansion (MilNOD IV)			
<b>Principal Investigator:</b> Lori A. Loan, RNC, PhD			
<b>Department:</b> Nursing		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Patricia A. Patrician, AN; COL Laura R. Brosch, AN			
<b>Start - Completion:</b> 8 Apr 2004 - Aug 2005		<b>Funding:</b> Triservice Nursing Research Program via The Geneva Foundation	<b>Periodic Review:</b> 18 Dec 2007

**Study Objective:** This is the fourth study (MilNOD IV) in a program of research examining nurse staffing and patient outcomes. This particular study will shift from database development to examining aspects of structure, process, & outcome.

**Technical Approach:** Data deemed valid and reliable from the study, "Establishing a Military Nursing Outcome Database" (Brosch, 2002), will undergo secondary analyses to examine relationships between nursing structure indicators, and patient and nurse outcome indicators. The research team will specify a series of regression models, examining each outcome variable separately. For survey subscales on the Nursing Work Index-Revised and the Patient Satisfaction Survey, correlations will be performed to examine associations among independent variables and between independent and dependent variables. Simple Pearson's correlations will indicate whether a relationship exists between nurse and patient satisfaction.

**Progress:** This protocol has completed all data collection activities, but remains ongoing to clean and prepare the data set for statistical analysts from the California Nursing Outcomes Coalition to perform the requested analyses related to nurse staffing and nurse and patient outcomes in medical, surgical, medical/surgical, stepdown, and ICU environments in both small and large facilities. It is anticipated that this will take a minimum of two months. An abstract and final report will be prepared once the analyses are completed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204084	<b>Status:</b> Completed
<b>Title:</b> Impact of Inpatient Physician Order Entry on Medication Administration and Dispensing Error Rates in the Neonatal Intensive and Intermediate Care Units		
<b>Principal Investigator:</b> Lori A. Loan, RNC, PhD		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Donna C. Whitney, MC; James A. Taylor, M.D.; Susan Blackburn, Ph.D., RNC		
<b>Start - Completion:</b> 14 Jun 2004 - Jun 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 20 May 2006

**Study Objective:** The proposed study will be conducted in two phases. Phase One is designed to pilot test an observational methodology called Line Operator Safety Audit (LOSA) and modify LOSA for use with medication error detection in the NICU/ICN and inpatient pharmacy. Phase One will also include refinement of data collection instruments and techniques. Once the optimal observation techniques and data collection instruments are determined, Phase Two will begin. In this phase the number and types of observed medication administration and dispensing errors will be compared before and after inpatient physician order entry is initiated in the NICU/ICN at Madigan Army Medical Center.

**Technical Approach:** This study will examine medication errors before and after the initiation of inpatient physician order entry (IPOE) in the Neonatal Intensive Care Unit (NICU) or Intermediate Care Nursery (ICN), and point out what types of errors are common in this patient population. Approximately 25 health care personnel dispensing (pharmacy personnel) or administering (nursing personnel) medications for NICU or ICN patients will be watched until approximately 750 opportunities-for-error have been observed. The study will use a pretest-posttest design and appropriate statistical techniques (t-test, Mann Whitney U or chi-square) to compare medication administration and dispensing error rates from two data collection periods- 1-month before NICU/ICN IPOE begins and 4 months after NICU/ICN IPOE is initiated. Information from the study will be used to develop practical error-prevention strategies.

**Progress:** This protocol was reported as completed in April 2007. Results: Rates of variance before, and after, implementation of Computer Physician Order Entry (CPOE) in the NICU were compared using negative binomial regression; patient census and acuity level on each observation day were included in the model. Specific types of, and reasons for, medication variances in the pre-CPOE and CPOE periods were also compared. Data on 526 medication administrations were collected, including 254 during the pre-CPOE period and 272 after implementation of CPOE. Medication variances were detected during 19.8% of administrations during the pre-CPOE period as compared to 11.6% after CPOE was implemented (rate ratio 0.53, 95% confidence interval 0.33, 0.84). Overall, administration mistakes, prescribing problems, and pharmacy problems accounted for 74% of medication variances; there were no statistically significant differences in rates for any of these specific reasons before, or after, CPOE was introduced. Among different types of variances, administration of a medication at the wrong time accounted for 53.1% of all variances. Variances related to giving a drug at the wrong time were significantly lower during the CPOE period than in the pre-CPOE period (rates 6.7% and 9.9% respectively, rate ratio 0.53, 95% confidence interval 0.29, 0.99). The implementation of CPOE in a NICU was associated with a significant decrease in the rate of medication administration variances. However, even with the use of CPOE, a variance was noted during more than 11% of all medication administrations, suggesting that additional methodologies may be needed to improve neonatal patient safety.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205037	<b>Status:</b> Ongoing
<b>Title:</b> Determining the Effectiveness of a Stroke Prevention Program		
<b>Principal Investigator:</b> Lori A. Loan, RNC, PhD		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Mona O. Bingham, AN; LTC Jon C. Allison, MC; Nancy A. Cox, RN, BSN; Samuel C. Sorbello, RN		
<b>Start - Completion:</b> 3 Feb 2005 - Jan 2011	<b>Funding:</b> DCI	<b>Periodic Review:</b> 11 Sep 2007

**Study Objective:** To determine the effectiveness of an intensive one-on-one case management program designed to control identified risk factors for stroke and reduce the incidence of stroke in target population.

**Technical Approach:** This longitudinal study will use a randomized, two group repeated measures design to compare a nurse case management stroke prevention program to standard care provided by primary care services in order to determine the effectiveness of an intensive 1:1 case management intervention. After one year there may be a cross-over group of those control subjects who wish to enter the case management intervention program. The study's primary outcomes are blood pressure, LDL, HgA1c, and BMI (as calculated from measures of height and weight). Secondary outcome measures include including incidence of vascular events, hospitalizations, emergency room visits, progression of carotid artery disease, control of atrial fibrillation, tobacco cessation and decreased tobacco use, and exercise level. Quality of life, mental wellness, and overall health will also be measured through approved survey instruments available on the MAMC web system.

Medical information from case management visits, medical records, hospital information, and health instruments will be used to compile data for this study. Chi-square, t-tests, ANOVA with repeated measures, and Mann-Whitney U tests will be used to compare group outcomes. The actual 1:1 case management intervention will last one year. At the end of one year, each patient will be re-evaluated to determine if case management services are still needed. At this time, control patients will be asked if they would like to receive case management services until capacity is reached for case management load. Results will be analyzed at 6 months, 1 year, and for 5 years there after for study subjects.

**Progress:** All data has been collected from 187 charts; however, data analysis has been delayed due to the PCS of the original PI. The protocol remains ongoing at MAMC to allow LTC Bingham a chance to return to the area to retrieve the study records and complete data analysis.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205117	<b>Status:</b> Completed
<b>Title:</b> A Qualitative Descriptive Study that Identifies Essential Competencies and Leadership Characteristics of Army Adult Medical-Surgical Critical Care Head Nurses (dissertation)		
<b>Principal Investigator:</b> Lori A. Loan, RNC, PhD		
<b>Department:</b> Nursing		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Roy A. Harris, AN		
<b>Start - Completion:</b> 29 Jul 2005 - May 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 2 Jul 2007

**Study Objective:** The purpose of this study is to identify and describe competencies and leadership characteristics of Army Adult Medical-Surgical Critical Care Head Nurses. The research questions are: (1) what are the essential competencies and leadership characteristics identified by Army Critical Care Head Nurses themselves, (2) what are the essential competencies and leadership characteristics of Army Critical Care Head Nurses identified by Army critical care staff nurses, (3) what are the essential competencies and leadership characteristics of Army Critical Care Head Nurses identified by Army Chief Nurses, and (4) what common essential competencies and leadership characteristics of Army Critical Care Head Nurses do these three levels of professional nursing identify?

**Technical Approach:** This is a qualitative, descriptive study semi-structured interviews that include both closed-ended and open-ended questions as the primary means of data collection. Five Army Nurse Corps nurses will be asked to participate at MAMC; the Chief Nurse, one Critical Care Head Nurse, and three Critical Care staff nurses. Total study subjects from all sites will be 35; 5 nurses each from Walter Reed Army Medical Center, Landstuhl Regional Medical Center, Dwight David Eisenhower Army Medical Center, Tripler Army Medical Center, Brooke Army Medical Center, William Beaumont Army Medical Center, and Madigan Army Medical Center. The associate investigator will conduct the interviews in all seven medical centers and at all echelons. Documented informed consent will be obtained to allow subjects to decline enrollment. The consent process will not be conducted by the associate investigator who will be conducting the interviews.

Demographic data will be collected which will serve as a descriptive framework during the analysis phase of the study. Frequencies and measures of central tendency will be utilized to analyze the respondent's demographic data. Other analyses will be conducted using descriptive qualitative methodology. Qualitative analysis of the data will be completed with a focus on a comprehensive description of essential competencies and leadership characteristics of Army Critical Care Head Nurses as perceived by the three echelons of respondents. To ensure that ongoing analysis occurs throughout the study, the modality of constant comparative analysis will be utilized. The data will be organized by transcribing the audiotapes of the interviews into the Microsoft word processing program. The transcriptions will be entered into the computer program, NVivo to facilitate the coding process. Information gleaned from this study will be de-identified and aggregated and used as part of the associate investigator's dissertation requirement at George Mason University. Findings will also be offered to the Army Nurse Corps, presented at nursing conferences and published in a national nursing journal.

**Progress:** This protocol was reported as completed in September 2007. Five interviews were conducted at MAMC, and 26 interviews were conducted at other Army MTFs. There were five themes that emerged from the interviews with these 31 research participants: (1) The Army Critical Care Head Nurse (ACCHN) is the clinical and subject-matter expert for their unit staff and the critical care consultant to the Chief Nurse; (2) The ACCHN is the role model for the entire critical care staff and leads their staff by example; (3) The ACCHN needs to possess

communication and interpersonal skills that foster a positive environment for patient care, professional growth and development of Army Nurse Corps Officers; (4) The ACCHN honestly and candidly advocates for their critical care unit, patients and staff to all other health care providers who practice in their unit as well as the departmental and organizational leadership; (5) The ACCHN who thoroughly knows their critical care staff nurse in terms of professional and personal lives provides a critical care unit environment where critical care nurses provide quality patient care, thrive professionally and want to continue to practice and are retained in this critically short profession.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207063	<b>Status:</b> Completed
<b>Title:</b> Patient Perceptions, Attitudes and Barriers to Using Water for Comfort in Labor and Birth (Pilot Study)		
<b>Principal Investigator:</b> Lori A. Loan, RNC, PhD		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Tanya M. Foster, AN		
<b>Start - Completion:</b> 23 Feb 2007 - Jan 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study will be to collect information about women's birthing preferences, knowledge and desires for using hydrotherapy (water for coping and comfort during labor and/ or birth) during their birth process. Specific descriptive information about women's choice and preference to use water in her labor and/or birth will be sought using qualitative interviews.

**Technical Approach:** In a military setting it is important that women receive comparable care to what they would receive in the civilian community, including choices for labor and birth. It is equally important that care providers in military settings understand the care preferences and perceived needs of their patient population. The birth process is an extremely important time in a woman's life that can impact her, her family and her child. The use of water or hydrotherapy is one non-pharmacological measure used throughout history by women in labor to help reduce pain and provide comfort in the birth process. Although the reported benefits of labor and birth and water are many, there are limited controlled studies to support these claims. In addition to the limited amount of research that is done on the use of water for labor and birth, there is an equally scant amount of research done to investigate women's access to a choice of coping methods for labor discomfort, the actual decision-making process in that choice, and the actual pattern of use of the method.

This non-intervention study is designed to provide information only, about how women perceive using water for comfort in their labor and or birth process. This two-part pilot descriptive qualitative study uses anonymous questionnaires and taped interviews of pregnant women affiliated with a military treatment facility (as beneficiaries or dependents) about their interest in, perceptions of, and knowledge about use of water for comfort during labor and delivery. Two hundred (200) anonymous questionnaires will be collected from participants age 18 and older who are in their 12-40th week of their uncomplicated pregnancy. Fifteen (15) interview participants will be randomly selected from the questionnaire participants that have volunteered to complete the interview portion of the study. Data will be entered into SPSS for descriptive analysis including frequencies, measures of central tendency and standard deviation. Qualitative data will be analyzed for themes and overall content. The results of the study will provide information for providers and administrators about what their patient population is seeking in terms of labor and birth choices. In addition, findings will offer guidance for determining educational information and budgeting necessary to provide birthing tubs or other means of providing hydrotherapy.

**Progress:** This minimal risk protocol was initially approved by the Expedited Review Committee on 23 February 2007. Protocol is now complete.

**Results:** The study participant's knowledge of using water in the labor and birth process was high; 81% of the study respondents had heard of using water in the labor and birth process. Over 16% knew someone that has used water in their labor and birth. Most of the information and knowledge base comes from the Internet, television and friends and family, not healthcare

professionals. The number of first time mothers was almost equal to those having their second or subsequent child.

Of those that had a previous pregnancy and birth, over half used an epidural for pain management in their birth experience, almost 6% had used water for comfort during their previous labor and none of the study participants had experienced a waterbirth. There were no significant statistical differences in the answers provided between the groups based on age, parity, education race/ethnicity or military status. Over 90% of the participants had not discussed the use of water as an option in their labor and or birth and their providers did not offer or discuss the option of using water in their labor with them. When asked if they would consider laboring or giving birth in water almost an equal number of participants strongly agreed that they would or would not, with the modal response being neutral or unsure. When asked if they would need more information before considering using water as an option in their labor and birth there was strong agreement that indeed they would like/need more information about the option. When questioned about the safety of using water in labor and/or birth over half of the participants agreed or strongly agreed that it is safe. Results of the interview portion of the study revealed several themes. There was an overall positive perception of the use of water in labor and birth. Most participants would be open to using water for comfort in their labor instead of or prior to other pharmacological methods of pain relief. There is a resounding belief that the option to use hydrotherapy be provided and that it be discussed and educational materials provided. There is also a need for more information needed to help make the decision to use. Barriers included provider discussion, patient knowledge base and institutional restrictions. There were no statistically significant differences in the answers accounting for the differences in age, military status and parity. First time mothers tended to rank the use of water in labor and birth more positively in aspects of effectiveness and safety.

**Conclusions:** The results of this study clearly indicate that there is interest in the use of hydrotherapy in the labor and birth process being available to DOD beneficiaries. Participants had knowledge of the use of water in the labor/birth process, but their information was limited to sources other than healthcare workers. Participants believed that information should be provided and discussed by their provider and that the option to use water during labor and birth is an option that should be available to every women receiving care at the facility.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207120	<b>Status:</b> Ongoing
<b>Title:</b> Comparison of Cardiovascular Risk Factors in Deployed Military Personnel		
<b>Principal Investigator:</b> Lori A. Loan, RNC, PhD		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Leigh McGraw, RN, AN		
<b>Start - Completion:</b> 28 Sep 2007 - aug 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The overall objective of this study is to understand the role of cardiovascular (CV) and lifestyle risk factors on military personnel's CV health. The primary aim of this study is to compare CV risk factors between service members medically evacuated from Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) for ACS and CVA and a matched sample of deployed service members without ACS and CVA. Secondary aims of this study are to assess the accuracy of the Framingham risk score in stratifying deployed service members with and without ACS and CVA and assess the association between level of stress in theater and ACS and CVA.

**Technical Approach:** The design is a case control study, and the sample consists of 100 cases obtained through a retrospective record review out of Landstuhl Regional Medical Center, Germany, and 200 healthy matched controls obtained from the Soldier Readiness Processing site at Fort Lewis, WA. The independent variables in this study include: systolic and diastolic blood pressure (SBP/DBP) (mmHg), total cholesterol (mg/dl), low density lipoprotein cholesterol (LDL-C) (mg/dl), high density lipoprotein cholesterol (HDL-C) (mg/dl), very low density lipoprotein cholesterol (VLDL-C), triglycerides (TG) (mg/dl), BMI (kg/m<sup>2</sup>) as calculated from height and weight, fasting blood sugar (mg/dl), smoking status, composite "GWOT Stress Score" (0-10) (2 scores for "controls" to establish reliability using test-retest method), 3 subscales from the "Deployment Risk and Resiliency Inventory (DRRI)" (for controls only to establish criterion validity of "GWOT Stress Score") and Framingham risk score (FRS) (%). Controls will also have waist circumference (inches), Lp(a), HDL-2, HDL-3, IDL, and VLDL-3 obtained as part of the VAP test. The independent variables for the cases will come from a record review, including electronic sources, and for the cases, will consist of an interview, record review (including electronic sources) and blood draw. Analysis using conditional logistic regression will use these variables to predict the outcome variable of acute CV event.

**Progress:** This greater than minimal risk protocol received initial IRB approval on 28 August 2007. Final approval to initiate subject enrollment was received 28 September 2007.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207032	<b>Status:</b> Ongoing
<b>Title:</b> Bone Health in Soldiers Before and After Deployment		
<b>Principal Investigator:</b> Mary S. McCarthy, PhD		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Lori A. Loan, RNC, PhD; LTC Melinda L. Jackson, FNP; COL Curtis J. Hobbs, MC; Colleen Cates-Gorang, R.D., CDE		
<b>Start - Completion:</b> 7 Mar 2007 - Jun 2008	<b>Funding:</b> DEXA via Geneva Foundation	<b>Periodic Review:</b> 11 Dec 2007

**Study Objective:** Specific Aim #1: to determine the feasibility of quantifying calcium sweat loss in male and female soldiers in a hot desert climate under conditions of intense physical training. Specific Aim #2: to examine the significance of calcium loss on short-term bone health using biochemical markers of bone formation and resorption, as well as dual-energy x-ray absorptiometry (DEXA) to assess bone mineral quality. Specific Aim #3: to describe the potential impact of self-reported exercise and dietary habits on bone health of male and female soldiers.

**Technical Approach:** This prospective, descriptive, longitudinal pilot study will recruit 50 male and female Soldiers who will train at the National Training Center for the sweat collection necessary for calcium analysis. An additional 50 male and female Soldiers will be recruited from Ft. Lewis to participate in the pre- and post-deployment phases that look at physical exam findings, DEXA scans, biomarkers in blood and urine, and survey responses. Biochemical markers of bone turnover, as well as dual-energy x-ray absorptiometry (DEXA), will be used to assess bone mineral quality. Issues regarding feasibility will include the ability to recruit and retain sufficient eligible Soldiers, the ability to collect all specimens to include serum and urine bone turnover markers, sweat for calcium quantification, and DEXA scans at baseline and one year post-deployment. Sweat collection will be done using the Rianon et al. sweat patch method during scheduled physical training in a desert climate. Biochemical markers of bone formation and resorption include osteocalcin, P1CP, and ICTP which will be measured in serum by a radioimmunoassay. Peptide bound N-telopeptide crosslinks (NTX) will be measured by immunoassay in the urine as a specific marker of bone resorption. Soldiers will complete the Baecke Habitual Physical Activity and the Block 2005 Food Frequency Questionnaires. Data analysis will include descriptive statistics using mean + SD to report sample demographics and t-tests to examine baseline and post-deployment biochemical markers and DEXA results. Study findings will help determine if sweat calcium loss is sufficient to warrant a clinical trial that includes calcium supplementation for Soldiers

**Progress:** This minimal risk protocol was initially approved by the IRB on 12 December 2006, and received final approval 7 March 2007. A protocol amendment was submitted and approved to increase subject enrollment numbers and to correct the time of Soldier's deployment from one year to 15 months. Of the 52 male and female Soldiers enrolled only one was dropped due to non-deployable status (pregnancy identified by study UA). Soldiers were scheduled according to their deployment timetable; some deployed in July 2007 and others will depart in November 2007. All baseline data collection including physical exams, blood tests for bone turnover markers and endocrine markers, DXA for bone density, and questionnaires that examine diet and exercise habits were completed on October 2007. Phase II will be conducted at the NTC in Spring 2008 and Phase III will begin as soon as the first group of Soldiers in the original study sample re-deploys to Fort Lewis in October 2008.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206108	<b>Status:</b> Completed
<b>Title:</b> Army Nurse Corps Officers' Deployment Experiences and Reintegration		
<b>Principal Investigator:</b> COL Laurie A. McNabb, AN		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Lori A. Loan, RNC, PhD; LTC Denise Hopkins-Chadwick, AN; Mary S. McCarthy, PhD		
<b>Start - Completion:</b> 10 Jul 2006 - Jun 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To explore the many factors that impact nurses' ability to perform their jobs during all phases of a deployment; prior to the deployment, during the deployment, and during the post-deployment phase. Outcomes of this study will serve as the basis for the development of the best strategies to support nurses prior to and following a deployment in order to facilitate the smoothest transition, between workplaces.

**Technical Approach:** Prospective Data Collection Procedures: Army Nurse Corps Officers will be recruited based on the inclusion criteria and availability. Nurses interested in participating in the study will be contacted by phone or email. During this initial call, one of the study investigators will discuss a variety of issues with each participant such as the study purpose, what will be needed from them as participants, who will be at the group or interview, and other specifics of the focus group sessions. They will be given information about the study and their questions will be answered. Those volunteering to participate will be scheduled for attendance at focus group sessions or interviews through telephone calls or personal interactions carried out 7 to 14 days prior to the session. To increase attendance, participants will again be contacted telephonically by a research team member 24 hours prior to the date and time of the session (Goldstein & McDonald, 1987; Krueger, 1988; Stewart & Shamdasani, 1990). Participants will also be given a demographic data collection sheet and asked to complete it and bring it to the focus group meeting. These sheets will be collected from participants after consenting is complete. If participants fail to bring the sheet, they will be asked to supply demographic information at the time of the focus group session.

**Progress:** This protocol was completed during FY07. A total of 12 subjects participated in one of 3 focus groups that were held last spring at the Battle Command Training Center. The data has been analyzed. There were no adverse events. The study is complete. Results are as follows: Major Contributing Factors: Leadership: was found to be a major reason for prematurely leaving military service. The overall retention theme was that if you have good leadership, it affects everything and that they will want to stay in the ANC through good times or bad whether it's through war or peace because of the leadership. Deployment Length: Another major deployment related retention issue was the length of deployment. Resoundingly the participants noted that shortening the duration of deployment would greatly increase retention with the recommended length being somewhere between 6-9 months. Minor Contributing Factors: Predeployment Training and Unit Cohesiveness: The overall retention theme for pre-deployment training and unit cohesion was "transform pre-deployment training so it matches the reality of the deployed environment and allows the unit to function as a team". Redeployment Treatment: The overall retention theme for the redeployment treatment was "Make honest efforts to give assignments that move us forward in our career, treat us like you want us to stay in, evaluate post-deployment health, co-locate us on work units, suggest Army OneSource, & recognize us with a welcome home".

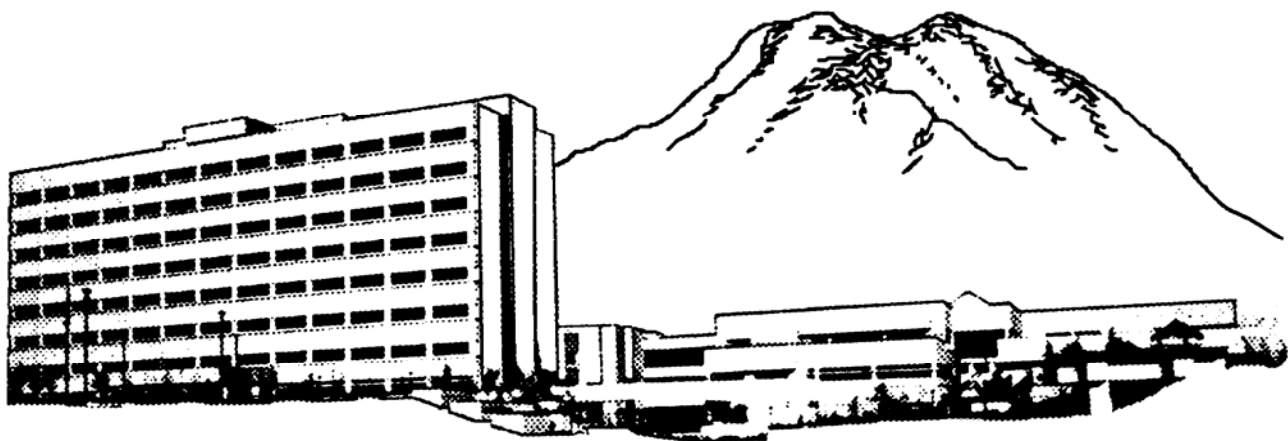
### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206107	<b>Status:</b> Ongoing
<b>Title:</b> Menstruation During Deployment: Women's Attitudes Towards Menstrual Suppression		
<b>Principal Investigator:</b> LTC Lori L. Trego, AN		
<b>Department:</b> Nursing		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Lori A. Loan, RNC, PhD; LTC Denise Hopkins-Chadwick, AN; 1LT Sandra L. Gordy, AN		
<b>Start - Completion:</b> 10 Jul 2006 - Aug 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 12 Jun 2007

**Study Objective:** Objective is to perform instrument development and testing of a military-specific measure of the experience of menstruation and associated attitudes towards menstrual suppression in a deployed environment. Specific Aims are to (1) establish the reliability (internal consistency) of an instrument that measures military women's experiences of menstruation and attitudes towards menstrual suppression and (2) establish the validity (content, face, construct, convergent, discriminant) of an instrument that measures military women's experiences of menstruation and attitudes towards menstrual suppression.

**Technical Approach:** Data collection will be the administration of a paper and pencil survey consisting of the Military Women's Attitudes Towards Menstrual Suppression, the Attitudes Towards Menstrual Suppression Scale (ATMS), the Menstrual Attitudes Questionnaire (MAQ), and a Deployed Menstrual Health Practice Questionnaire (DMHPQ). Targeted sample size per power analysis is 300-500 participants, as required for factor analysis. Psychometric testing with this sample size allows for tests of internal consistency and item evaluation in the assessment of reliability as well as exploratory factor analysis for construct validation. Several methods of construct validity have been chosen for this study: content validity, face validity, construct validity, and convergent and discriminant construct validity. The sample will therefore complete a questionnaire that consists of the MWATMS, as well as two other valid instruments that will be used to test convergent and discriminant validity: the Menstrual Attitude Questionnaire (MAQ) and the Attitudes Towards Menstrual Suppression scale (ATMS).

**Progress:** This minimal risk protocol began enrollment and data collection 25 October 2006. Preliminary results were presented at Madigan Research Day 2007. This study is part of a dissertation requirement for PhD Nursing Science at University of Washington with a completion date set for August 2007. The protocol remains ongoing pending completion of the final manuscript.



## **Detail Summary Sheets**

Department of Obstetrics/Gynecology

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205140	<b>Status:</b> Terminated
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**Title:** Continuous Use of the Oral Contraceptive for Menstrual Cycle Suppression and the Effects on Bone Density; a Prospective, Randomized, Clinical Trial

**Principal Investigator:** LTC Michael K. Chinn, MC

<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC
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**Associate Investigator(s):** Leslie Miller, M.D.; LTC Antonio G. Balingit, MC; Nancy A. Poffenberger, PAC, Ph; COL Diane M. Flynn, MC; LTC Wendy Ma, MC; LTC Jeffery L. Clemons, MC; COL Jon A. Proctor, MC; Gregory E. Chow, MD; CPT Tammy J. Mantzouris, MC; CPT Andrew E. Fong, MC

<b>Start - Completion:</b> 13 Jan 2006 - Dec 2011	<b>Funding:</b> DCI	<b>Periodic Review:</b> 19 Oct 2006
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**Study Objective:** To identify the dose of ethinyl estradiol (EE) in combination with levonorgestrel (LNG) or norethindrone acetate (NETA) that, when taken daily, results in rapid and sustained amenorrhea over two years with minimal changes in bone density.

**Technical Approach:** This study looks at what pill dose, when taken every day, will work the fastest to stop all period bleeding and which dose will keep the bleeding away for two years of daily use. Women will provide a monthly report of pill use and bleeding and have their bone density measured at baseline and after two years to see if the two estrogen doses or two progestin types will vary these and other safety effects. In addition, women stopping the study drug will be followed until menstruation returns to document reversibility. Female soldiers need to know which dose of birth control pill can induce menstrual cycle suppression, the safety of taking these pills every day for up to 2 years, the effects of an induced amenorrhea on their bone density, and the time it takes for menses to return following suppression.

**Progress:** There was no activity on this protocol during FY07, and the research eventually terminated when funds in support of the protocol could not be obtained.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 81035	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0041: Surgical Staging of Ovarian Carcinoma		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 16 Jan 1981 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 26 Nov 2007

**Study Objective:** To determine the spread of ovarian carcinoma to intraperitoneal structures and retroperitoneal lymph nodes by direct examination, cytologic sampling, and biopsy; to establish a surgical protocol for patients entered into GOG ovarian cancer treatments protocols; to determine the complication rate of the procedures.

**Technical Approach:** This protocol is being performed as a statistical protocol on patients who have surgery as standard treatment. Eligible patients will be those who have Stages I, II, or III ovarian carcinoma. Patients undergoing total abdominal hysterectomy, bilateral or unilateral salpingo-oophorectomy, bivalving of the ovary, selective pelvic and para-aortic lymphadenectomy, omental biopsy, or peritoneal cytology sampling will be studied. They will not be given any preoperative treatment, but will be subjected to a complete and thorough evaluation before surgery. All patients will be explored and the steps for surgery will be as standard surgery dictates. Specific observations will be made as to the findings. If fluid is not present, washings will be taken from the inside of the abdomen to study cells. A thorough examination of all structures from the diaphragm to the pelvic floor will be carried out. After surgical staging, patients will be transferred to the appropriate treatment protocol or to standard treatment if no protocol is available.

**Progress:** This protocol closed enrollment in February 1987, with thirteen subjects enrolled. Three subjects remain disease free and continued to be followed at MAMC during FY07. Final analysis of this trial appeared in the January 1988 GOG Statistical Report. The manuscript derived from this trial was published in Surg. Gynecol. Obstet 1989.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 81105	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0052: A Phase III Randomized Study of Cyclophosphamide Plus Adriamycin Plus Platinol Versus Cyclophosphamide Plus Platinol in Patients with Optimal Stage II Ovarian Adenocarcinoma		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 21 Aug 1981 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 26 Nov 2007

**Study Objective:** To determine, in optimal Stage III ovarian adenocarcinoma, if the addition of adriamycin to cyclophosphamide plus cis-platinum improves progression-free interval, frequency of negative second-look laparotomy and survival. This protocol replaces GOG 0025.

**Technical Approach:** Eligible patients are those more than six weeks post-operative with proven primary Stage III ovarian adenocarcinoma confined to the abdominal cavity and its peritoneal surfaces with residual tumor masses after surgery no larger than 1 cm in diameter. Patients with prior chemo or radiotherapy are ineligible. Patients will be randomized to cyclophosphamide plus Platinol every three weeks for eight courses or to cyclophosphamide and Platinol plus adriamycin every three weeks for eight courses. After eight courses those with less than clinically complete response will go off study and be followed for survival; those with clinically complete response will have second-look surgery to validate the complete response or to remove residual tumor masses. Patients will then be followed for approximately five years for survival rates.

**Progress:** This protocol closed enrollment in July 1985, with six subjects enrolled. One subject remains disease free and continued to be followed at MAMC during FY07. Final analysis of the study appeared in the July 1988 GOG statistical report. Seven abstracts and publications (listed in the GOG statistical report) evolved from this clinical trial.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 84033	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0072: Ovarian Tumors of Low Malignant Potential: A Study of the Natural History and a Phase II Trial of Melphalan and Secondary Treatment with Cisplatin in Patients with Progressive Disease		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 17 Feb 1984 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 26 Nov 2007

**Study Objective:** To evaluate the biologic behavior of ovarian tumors of low malignant potential; to evaluate the effectiveness of chemotherapy against this disease (initially, a Phase II study of melphalan); and to evaluate the response rate to cisplatin in melphalan failures.

**Technical Approach:** Patients without prior chemotherapy of radiotherapy who have had adequate surgical staging will be eligible. Patients with no grossly visible residual disease will receive no treatment and be followed for five years if there is no subsequent disease. If there is no grossly visible clinically apparent residual for 12 months, the patients will have second look surgery and then proceed to melphalan treatment (5 days every four weeks) or follow-up (complete response). With progression after melphalan, patients will proceed to third look and cisplatin treatment (once every three weeks for eight weeks) or follow-up. If there is no evidence of response after three courses of cisplatin, the treatment will be discontinued. Patients who have progression during the first 12 months will be treated as above except they will proceed directly to melphalan treatment without second look surgery. Follow-up will be for a minimum of five years with clinical examination every three months for the first two years, then every six months thereafter.

**Progress:** This study closed enrollment in February 1992, with ten subjects enrolled. Three subjects have been lost to follow-up, two with no evidence of disease are followed out-of-state, and five continued to be followed at MAMC during FY07. Statistical analysis appeared in the July 2002 GOG Statistical Report. Manuscript derived from this trial was published in JCO 1995.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 84074	<b>Status:</b> Completed
<b>Title:</b> GOG 0078: Evaluation of Adjuvant VP-16, Bleomycin, and Cisplatin (BEP) Therapy in Totally Resected Choriocarcinoma, Endodermal Sinus Tumor, Embryonal Carcinoma and Grade 3 Immature Teratoma of the Ovary, Pure and Mixed with Other Elements		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 17 Aug 1984 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 21 Sep 2006

**Study Objective:** To evaluate the effect of adjuvant vinblastine, bleomycin, and cisplatin (VBP) chemotherapy in patients with endodermal sinus tumor and choriocarcinoma of the ovary (pure and mixed) after removal of all gross tumor; to evaluate the role of serum markers, especially alpha fetoprotein and HCG, in predicting recurrence; to evaluate the role of reassessment laparotomy in determining response, detecting early relapse, and planning further therapy; and to compare the biologic behavior of pure endodermal sinus tumors with mixed germ cell tumors containing endodermal sinus elements. Per addendum of Jan. 87: to evaluate the acute and chronic toxicity of this chemotherapy on gonadal and reproductive function.

**Technical Approach:** Patients with totally resected Stage I choriocarcinoma, endodermal sinus tumor, or embryonal carcinoma of the ovary with negative peritoneal washings, normal (or falling at a rate that does not suggest residual disease) serum AFP and beta-HCG levels, and adequate bone marrow, renal, and hepatic function will be studied. Stages II and III will also be eligible if all gross tumor is resected. After recovery from surgery, patients will receive 3 cycles of VBP therapy. Patients who show evidence of progression while on VBP therapy will be candidates for GOG Protocol 26. Patients completing three cycles of treatment clinically free of disease will undergo reassessment laparotomy. Patients with recurrent disease at reassessment laparotomy will be candidates for GOG Protocol 26. To be eligible a patient will receive at least one week of chemotherapy and live another two weeks. Each patient will remain on study until adverse effects prohibit further therapy or until evidence of progression is noted. Per addendum of Jan. 86: the title has been changed as shown above; vinblastine has been replaced by VP-16; Grade 3 immature teratoma has been added for entry and evaluation.

**Progress:** This protocol was reported as completed in FY07. The study closed enrollment in February 1992, with one subject enrolled who was followed out of state until lost to follow-up in FY02. Final analysis of this study appears in the July 1993 GOG Statistical Report. Manuscripts derived from this clinical trial published in 1994.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 86089	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0085: A Randomized Comparison of Hydroxyurea versus 5-FU Infusion and Bolus Cisplatin as an Adjuvant to Radiation Therapy in Patients with Stages II-B, III, and IV-A Carcinoma of the Cervix and Negative Para-Aortic Nodes		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 19 Sep 1986 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 26 Nov 2007

**Study Objective:** To determine whether hydroxyurea or the combination of 5-FU and cisplatin is superior as a potentiator of radiation therapy in advanced cervical carcinoma and to determine the relative toxicities of hydroxyurea versus the combination of 5-FU and cisplatin when given concurrently with radiation therapy.

**Technical Approach:** Patients with invasive squamous cell, adenocarcinoma, or adenosquamous carcinoma of the cervix, Stages II-B, III, and IV-A, who meet the eligibility requirements as listed in the protocol, will undergo clinical staging as permitted by FIGO rules. All patients will undergo surgical staging to include extraperitoneal sampling of the para-aortic lymph nodes, peritoneal cytology, and intraperitoneal exploration. Patients with cancer confined to the pelvis will receive pelvic irradiation and will be randomly assigned to receive either concomitant 5-FU and cisplatin or hydroxyurea. Patients with disease outside the pelvis are not eligible for this protocol. The study will continue as long as treatment protocols remain activated. The patients will be followed for two years and then every six months for three additional years.

**Progress:** This protocol closed enrollment in December 1990, with two subjects enrolled. One subject has been lost to follow-up since 1985, and the other subject remains disease free and continued to be followed at MAMC during FY07. Final statistical analysis appeared in the July 1997 GOG Statistical Report. Two abstracts and a publication (listed in the GOG statistical report) have been derived from this clinical trial.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 87028	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0095: Randomized Clinical Trial for the Treatment of Women with Selected Stage IC and II (A,B,C) and Selected IAi and IBi and IAii and IBii Ovarian Cancer, Phase III		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 21 Nov 1986 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 26 Nov 2007

**Study Objective:** In definitively staged patients who have tumor involving one or both ovaries with pelvic extension and/or malignant ascites and/or positive peritoneal washings and in those Stage IAi and IBi patients with poorly differentiated tumors and stage IAii and IBii (all grades) to: compare the progression-free interval and overall survival of the two treatment regimens; determine the patterns of relapse for each form of therapy; and define the relative toxicities of the two treatment approaches.

**Technical Approach:** The study design will be a randomized comparison between the standard adjuvant treatment (P32) and an experimental arm of short term intensive adjuvant combination chemotherapy with cyclophosphamide/cisplatin in patients with ovarian cancer. One to two weeks following surgery, P32 therapy will be started. Fifteen millicuries of chromic phosphate suspension mixed in 500 cc of normal saline will be infused into the peritoneal cavity via the peritoneal dialysis catheter after a technetium scan or abdominal x-rays with contrast material has demonstrated adequate distribution. In order to facilitate distribution of the P32, the patient will be turned every 15 minutes to the left side, onto the back, in Trendelenburg and reverse Trendelenburg positions, onto the right side and so on for two hours following the infusion. Chemotherapy will consist of cyclophosphamide, 1 mg/m<sup>2</sup> I.V., on day 1 plus cisplatin, 100 mg/m<sup>2</sup> IV, on day 1 administered one hour after cyclophosphamide. Cycles of combination chemotherapy will be repeated every three weeks depending upon the time to recovery of the blood counts to pretreatment level. Cycles of chemotherapy will be repeated for a total of three cycles. Patient follow-up will continue until death, loss of follow-up, or termination of the study. Patients will remain on study until disease progression or adverse effects dictate otherwise. An adequate trial is defined as receipt of at least one course of therapy and one follow-up visit.

**Progress:** This protocol closed to enrollment in March 1994, with five subjects enrolled. One subject remains disease free and continued to be followed at MAMC during FY07. Final analysis of this trial appeared in the July 2000 GOG Statistical Report. Abstracts and manuscripts derived from this trial have been published as listed in the GOG Statistical Report.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 87091	<b>Status:</b> Completed
<b>Title:</b> GOG 0099: A Phase III Randomized Study of Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 17 Jul 1987 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 21 Sep 2006

**Study Objective:** To determine if patients with intermediate risk endometrial adenocarcinoma who have no spread of disease to the lymph nodes benefit from postoperative pelvic radiotherapy and to evaluate how the addition of pelvic radiotherapy will alter the site and rate of cancer recurrence in these intermediate risk patients.

**Technical Approach:** Patients with primary histologically confirmed Grade 2 or 3 endometrial adenocarcinoma (endometrioid, villoglandular, mucinous and adenosquamous) and clear cell carcinoma will be eligible. Patients must have had a total abdominal hysterectomy, bilateral salpingo-oophorectomy, selective pelvic and para-aortic node sampling, pelvic washings and found to be surgical Stage 1 with myometrial invasion. Following surgery, patients will be randomized to no additional treatment of pelvic radiation therapy to begin no later than eight weeks after surgery. Those randomized to radiation therapy will be treated with AP and PA parallel ports with each port being treated each day. A daily tumor dose of 180 cGy will be given to a total dose of 5040 cGY in approximately six weeks. Each patient will be followed with regular visits occurring every three months for the first two years, every six months for the third, fourth and fifth years, and yearly thereafter.

**Progress:** This protocol was reported as completed in FY07. The study closed enrollment in July 1995, with three subjects enrolled. One subject died and the other two have been lost to follow-up since 2003. Final analysis appeared in the January 1999 GOG Statistical Report. Two abstracts were published. Manuscript derived from this clinical trial is under revision for publication.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 87104	<b>Status:</b> Completed
<b>Title:</b> GOG 0092: Treatment of Selected Patients with Stage 1B Carcinoma of the Cervix After Radical Hysterectomy and Pelvic Lymphadenectomy: Pelvic Radiation Therapy versus No Further Therapy		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 21 Aug 1987 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 21 Sep 2006

**Study Objective:** To determine the value of adjunctive pelvic radiation in the treatment of Stage 1B carcinoma of the cervix but with selected high-risk factors; to determine the recurrence-free interval, survival and patterns of failure in those patients; and to determine the morbidity of adjunctive pelvic radiation following radical hysterectomy.

**Technical Approach:** All patients with Stage 1B cancer of the cervix who have been treated by radical hysterectomy and pelvic node dissection and found to have cancer confined to the cervix and who have a large tumor and/or lymph or blood vessel invasion in the cervix will be eligible to enter the study. Patients will be randomized to one of two groups. One group will receive external radiation therapy to the pelvis and the other group will receive no further therapy. Patients assigned to receive the radiation therapy will receive the therapy daily for 4 to 6 weeks. Both groups of patients will be required to have check-ups every three months for three years and then every six months for two more years.

**Progress:** This protocol was reported as completed in FY07. The study closed enrollment in December 1995, with one subject enrolled in FY88, but who has been lost to follow-up since 2005. Final analysis appears in the January 1999 GOG Statistical Report. An abstract and publication have been derived from this clinical trial.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 93063	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0123: A Randomized Comparison of Radiation Therapy & Adjuvant Hysterectomy vs Radiation Therapy & Weekly Cisplatin & Adjuvant Hysterectomy in Patients with Bulky Stage IB Carcinoma of the Cervix		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 6 May 1994 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 26 Nov 2007

**Study Objective:** To evaluate the addition of weekly chemotherapy with Cisplatin during radiation therapy in patients with bulky Stage IB carcinoma of the cervix.

**Technical Approach:** This study randomizes patients to two different treatment regimens. Both regimens include radiation therapy followed by hysterectomy. Regimen I - Radiation Therapy Plus Adjuvant Hysterectomy - Patients will undergo combined external and intracavitary radiation therapy followed by extrafascial hysterectomy (total doses of 13000 cGy). Regimen II - Radiation Therapy Plus Weekly Cisplatin Infusion Plus Extrafascial Hysterectomy. Patient will undergo radiation therapy to receive a total dose of 13000 cGy using a combination of external and intracavitary radiation therapy. Each week during external radiation therapy and during the intracavitary applications the patient will receive an infusion of cisplatin 40 mg/m<sup>2</sup> not to exceed 70 mg maximum in any single infusion, up to a maximum of 6 doses of cisplatin. Extrafascial hysterectomy will be carried out no later than six weeks following the last day of treatment in both regimens.

The principal parameters to determine the efficacy of weekly cisplatin during radiotherapy are: 1) Outcome variables (recurrence-free interval (RF), survival and local control rate); 2) Tumor characteristics; 3) Host characteristics; 4) Adverse effects; 5) Therapy administered.

**Progress:** This protocol closed enrollment in April 1997, with one subject enrolled who remains disease free and continued to be followed at MAMC during FY07. No adverse events or changes to the protocol were reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206029	<b>Status:</b> Ongoing
<b>Title:</b> Simulation Training for Postpartum Hemorrhage		
<b>Principal Investigator:</b> MAJ Shad H. Deering, MC		
<b>Department:</b> OB/GYN		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 14 Dec 2005 - Jan 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 26 Nov 2007

**Study Objective:** To have OB/GYN residents perform a simulated postpartum hemorrhage scenario to evaluate their clinical management skills and evaluate a standardized grading form.

**Technical Approach:** A standard postpartum hemorrhage simulation has been designed using the NOELLE mannequin and the new uterine hemorrhage model at the Anderson Simulation Center (designated for use by OB/GYN). Standardized objective and subjective evaluation sheets have been created to evaluate resident's performance. Prior to beginning the simulation, residents will be given a case scenario describing the patient's clinical situation. Residents will enter the room and address the active bleeding that is occurring. All simulations will be digitally recorded with at least two evaluators present to assess the resident's performance using the standard evaluation forms. Residents will be able to perform an examination and ask for medications to be administered. An empty syringe will be used by a staff member playing the part of the nurse to "administer" any medications requested and the resident will be made to clarify the dose and route of the medication. The simulation will end when the resident has performed an appropriate physical examination, fundal massage, and administered two medications in the correct dose and route, or when a total of 5 minutes has expired. After the simulation, the resident will be shown their grading scores and additional instruction will be performed in any areas that were deficient.

**Progress:** This protocol closed to enrollment with 14 total subjects enrolled during FY06. The study remains ongoing to complete data analysis. No changes to the protocol have been reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206098	<b>Status:</b> Terminated
<b>Title:</b> Serum Estradiol Levels in Patients with Polycystic Ovarian Syndrome undergoing Ovulation Induction with Clomiphene Citrate		
<b>Principal Investigator:</b> CPT Shannon K. Flood, MC		
<b>Department:</b> OB/GYN		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Jon A. Proctor, MC		
<b>Start - Completion:</b> 5 Jun 2006 - May 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To correlate serum estradiol levels and ovulation rates in patients with polycystic ovarian syndrome undergoing ovulation induction with clomiphene citrate.

**Technical Approach:** This is a prospective observational study to analyze the relationship between serum estradiol levels and ovulation rates in women with polycystic ovarian syndrome undergoing ovulation induction with clomiphene citrate. Women enrolled in the study will take 50-250 mg of clomiphene citrate on days 3-7 or days 5-9 of their menstrual cycle. They will also present for transvaginal ultrasound and a serum estradiol levels on menstrual cycle day 12, 13, or 14. Patients will be provided with urinary lutenizing hormone detection kits, and will be instructed to record the day of their LH surge. Lastly, patients will obtain a serum progesterone concentration seven days after their LH surge. This data will be organized in a spreadsheet format. The study participants will then be divided into two groups, those who ovulated and those who did not. Mean estradiol levels will then be calculated for each group. Appropriate post hoc statistical analysis will then be performed to evaluate for any correlation between estradiol levels and ovulation rates.

**Progress:** This protocol was terminated by the IRB as both the principal investigator and associate investigator no longer worked at MAMC. The last report was that ten subjects enrolled in FY07; two did not complete the laboratory tests as instructed. The number of subjects enrolled was not large enough to extract any significant findings or draw any conclusions.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204111	<b>Status:</b> Terminated
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**Title:** Glyburide Compared to Insulin in the Management of White's Classification A2 Gestational Diabetes

**Principal Investigator:** LTC Demetrice L. Hill, MC

<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC
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**Associate Investigator(s):** COL Peter G. Napolitano, MC; COL Peter E. Nielsen, MC; MAJ Jennifer L. Gotkin, MC; LTC Bobby C. Howard, MC, USAF; CPT Shannon K. Flood, MC; MAJ Andrea D. Shields, MC; LT Col. Damian J. Paonessa, MC, USAF

<b>Start - Completion:</b> 14 Dec 2004 - Mar 2006	<b>Funding:</b> Tripler AMC via MIPR	<b>Periodic Review:</b> 27 Feb 2007
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**Study Objective:** Pregnant women who meet the diagnostic criteria for gestational diabetes and fail dietary control will be randomized into two groups. One group will be prescribed glyburide and the other insulin in order to achieve optimal glucose control in pregnancy as manifested by decreased incidence of large for gestational age fetuses.

**Technical Approach:** This study will randomize 100 pregnant women into two groups, Group 1 will be prescribed glyburide and Group 2 will be prescribed insulin in order to achieve optimal glucose control in pregnancy as manifested by decreased incidence of large for gestational age fetuses. Subjects randomized into standard therapy insulin arm will have their insulin dose calculated by established standards. Insulin will be adjusted on a weekly basis in order to maintain optimal glucose control. Women assigned to receive glyburide will begin with 2.5 mg orally with the morning meal. Glyburide dosage will be increased weekly as indicated by the above threshold values to a maximum daily dose of 20 mg to achieve glucose control. If maximum daily dose of glyburide does not result in reaching the threshold values, patients will be administered insulin; however, data will be analyzed on an intent-to-treat basis. Continuous variables will be presented as mean +/- standard deviation, ordinal variables as medians, and dichotomous as percentages. Continuous data with normal distribution will be analyzed using unpaired (2sample) t-test. For more than 2 samples, analysis of variance (ANOVA, with possible repeated measures) will be used to analyze differences in outcome. Non-parametric equivalent tests will be used to compare ordinal variables or continuous variables not normally distributed. Categorical variables will be compared with the chi-square or Fisher exact test. Odds ratios will be calculated, with 95% confidence intervals. Logistic regression may be needed to adjust for confounding variables.

**Progress:** This protocol was terminated at MAMC in September 2007, due to enrollment difficulties. Of the eight subjects enrolled, three were randomized to Glyburide and five to insulin. No subjects on Glyburide had adverse reactions; however, two failed study treatment and were switched to insulin. Data collected under this protocol was in support of the parent protocol being conducted at TAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206099	<b>Status:</b> Ongoing
<b>Title:</b> Molecular mechanisms of progesterone mediated inhibition of LPS and other inflammatory agent induced production of pro-inflammatory cytokines in the fetal-maternal circuitry of the human placenta		
<b>Principal Investigator:</b> LTC Demetrice L. Hill, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LT Col. Damian J. Paonessa, MC, USAF; MAJ Jennifer L. Gotkin, MC; CPT Jeremy P. Celver, MS; Heidi M. Cederholm, B.S.; James R. Wright, BA, MT (ASCP); COL Peter G. Napolitano, MC		
<b>Start - Completion:</b> 16 Jun 2006 - Apr 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 21 May 2007
<p><b>Study Objective:</b> To identify the molecular mechanisms by which progesterone modulates pro inflammatory cytokine production following LPS and other inflammatory agent treatment of cells and tissue within the fetal/maternal circuit of the human placenta. Analysis will include ELISA, immunocytochemistry, western, antibody array, and high throughput proteomics.</p> <p><b>Technical Approach:</b> Placentas from normal women undergoing elective cesarean delivery prior to the onset of labor will be obtained within 15 minutes of delivery. At the time of cord clamping, 20cc of fetal cord blood will be obtained, spun down and the white blood cells collected and exposed to 50mg/ml lipopolysaccharide and evaluated using 1D or 2D gel electrophoresis. Additionally, both umbilical arteries will be gently and thoroughly flushed with Dulbecco's modified Eagle's medium (Gibco, Grand Island, NY) until the chorionic plate placental arteries are grossly free of blood. The arteries will be dissected from the placenta, carefully separating connective tissue from the endothelium. Eight contiguous segments of the umbilical artery (approximately 5 mm each) will be weighed and cultured in 6-well dishes (four per well) in either Hanks Balanced Salt Solution (HBSS) or Dulbecco's Modified Eagle's medium with Ham's F12 nutrient mixture (1:1) (DMEM/F12), antibiotics and 2 mmol/L glutamine in 5% carbon dioxide at 37C. Samples will be treated with 50ng/mL of lipopolysaccharide, lipopolysaccharide and medroxyprogesterone acetate (MPA) (50 ng/50 ng/ml), and MPA alone (50 ng/ml). Samples will be screened for total protein concentration by BCA analysis and specific induction of the inflammatory response by LPS will be verified with an Il6 or IL10 assay. Two placental explants from each group will be snap-frozen in liquid nitrogen and stored at -130C for possible total cellular proteomic analysis at a later date. The remaining placental explants will be stored in formalin at 4C and sectioned for immunohistochemical analyses as necessary.</p> <p>Total protein from equal volumes of supernatant will be separated by 1D or 2D gel electrophoresis with the assistance of Dr Robert Allen, PhD. Separated proteins will be labeled in gel by coomassie blue and silver staining. MALDI-TOF (40.00/protein) will be used to identify proteins with dissimilar expression patterns (e.g., a consistent change between LPS and control in 2/3 of the tested samples). Immunohistochemistry, western analysis of 2D gels with commercially-available antibodies and ELISA analysis will validate the proteomic analyses when feasible. A SELDI-based proteomic analysis will also be considered depending on the effectiveness of the gel electrophoresis.</p> <p><b>Progress:</b> Investigators have collected fetal cord blood and used waste maternal plasma from the Pregnancy Proteomic Study from 20 subjects over the last 12 months. Mononuclear cell populations have been isolated as described in the protocol and these cells evaluated for the presence of progesterone receptors. Cells have been exposed LTA and P4, and cell lysates for IL-6 secretion ultimately collected. This bench study remains on-going.</p>		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203066	<b>Status:</b> Ongoing
<b>Title:</b> The Production of Immunoregulatory Cytokines in a Placental Artery Explant Model		
<b>Principal Investigator:</b> LTC Bobby C. Howard, MC, USAF		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Peter G. Napolitano, MC; MAJ Christine M. Kovac, MC; MAJ Andrea D. Shields, MC		
<b>Start - Completion:</b> 30 Apr 2003 - Jun 2003	<b>Funding:</b> Air Force via MIPR	<b>Periodic Review:</b> 29 May 2007

**Study Objective:** To determine the production of inflammatory cytokines from the placenta vessels of normal patients following endotoxin stimulation.

**Technical Approach:** Levels of two distinct cytokines, IL-6 and IL-10 will be determined. IL-6 is a Th-1 type cytokine that is implicated in cell-mediated damage in clinical states characterized by an inflammatory response. In contrast, IL-10 is responsible for down-regulating the TH-1 like response and has been demonstrated to inhibit the damage related to inflammatory states. By understanding the production rate of these cytokines by placental arteries at baseline and under stimulated conditions, it will enable us to study the potential therapeutic modalities to suppress the production of inflammatory cytokines. Approximately 4 specimens will be examined here at MAMC.

**Progress:** This study closed enrollment in 2004 with a total of 11 subjects. The protocol remained ongoing during FY07 to complete data analysis.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203067	<b>Status:</b> Terminated
<b>Title:</b> The Effects of IL-10 on the Production of Inflammatory Cytokines in a Placental Artery Explant Model		
<b>Principal Investigator:</b> LTC Bobby C. Howard, MC, USAF		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Andrea D. Shields, MC; MAJ Christine M. Kovac, MC; COL Peter G. Napolitano, MC		
<b>Start - Completion:</b> 30 Apr 2003 - Jun 2003	<b>Funding:</b> Air Force via MIPR	<b>Periodic Review:</b> 20 Apr 2006

**Study Objective:** To determine the effects of IL-10 on placental artery production of inflammatory cytokines from normal patients.

**Technical Approach:** Maternal-fetal inflammatory states are associated with preterm labor, preterm premature rupture of membranes, preeclampsia, fetal growth restriction and fetal demise. It is also believed that cerebral palsy results from a fetal inflammatory response characterized by an environment of pro-inflammatory cytokines. IL-10 is a potent anti-inflammatory cytokine that has a potential role in the treatment of clinical septicemia by down-regulating the production of pro-inflammatory cytokines. Approximately 4 specimens will be studied here at MAMC.

**Progress:** This protocol was waiting on preliminary data from another study prior to initiation; however, the PI terminated the project prior to separating from the military, effective May 2007.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204088	<b>Status:</b> Ongoing
<b>Title:</b> Use of Transvaginal Cervical Length Measurements in Twin Gestations		
<b>Principal Investigator:</b> LTC Bobby C. Howard, MC, USAF		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Peter G. Napolitano, MC; Samantha J. Thomas, RN		
<b>Start - Completion:</b> 17 Sep 2004 - May 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 29 May 2007

**Study Objective:** To determine if the use of routine transvaginal cervical length ultrasound can be used to prevent preterm deliveries in twin gestations.

**Technical Approach:** Twin gestations are one of the highest risk populations for preterm labor and ideal to use in this prospective randomized clinical trial to determine if the use of transvaginal cervical length measures can be used to improve perinatal outcome and prevent unneeded intervention in women destined to deliver at term. Subjects will be randomized to either routine management or serial transvaginal ultrasound assessments of cervical length. Subjects randomized to cervical length assessment will be managed according to a set protocol based on cervical length. Potential management options will include expectant management, activity restriction, frequent nursing contact, and/or offering cerclage placement. The primary outcome analysis will compare gestational age at delivery between groups.

**Progress:** As of May 2007, a total of seven subjects enrolled in this study at MAMC, with no patients enrolled during FY07. Study data is being evaluated by study investigators.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203078	<b>Status:</b> Completed
<b>Title:</b> Use of Pipelle Endometrial Sampling in the Evaluation of Abnormal First Trimester Pregnancy		
<b>Principal Investigator:</b> CPT Alison L. Lattu, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Gregory E. Chow, MD; LTC Michael K. Chinn, MC; CPT Harlan I. Rumjahn, MC; CPT Joren B. Keylock, MC		
<b>Start - Completion:</b> 27 Aug 2003 - Sep 2004	<b>Funding:</b> DCI	<b>Periodic Review:</b> 10 May 2006

**Study Objective:** To evaluate the sensitivity of endometrial sampling in the detection of intrauterine products of conception in abnormal gestations.

**Technical Approach:** This study will look at patients undergoing evaluation and management for abnormal gestations who have opted for surgical management with dilation and curettage (D&C). This will not include patients undergoing emergency procedures. Approximately 100 patients will be enrolled into this study here at MAMC. The patient will have a pipelle endometrial sampling performed prior to the D&C. This procedure consists of a pipelle being inserted in to the uterine fundus and drawing it back and forth for 15-30 seconds to obtain a sample of the endometrial tissue and uterine contents. This sample will be transferred to a 10% formalin solution and then taken to the pathology department at MAMC for processing and evaluation.

**Progress:** Protocol reported as completed in May 2007. Results: Chorionic villi were detected by either biopsy or curettage in 26 of the 31 study participants. The remaining 5 subjects did not have chorionic villi detected on either specimen. The sensitivity of endometrial pipelle biopsy to detect chorionic villi was 73%. The sensitivity of curettage to detect chorionic villi was 92%. Conclusion: The sensitivity of curettage is superior to endometrial biopsy in detecting the presence of chorionic villi in abnormal gestations. However, the positive predictive value of endometrial biopsy may make this a useful tool in evaluating clinically stable patients with a presentation concerning for ectopic pregnancy in the office setting.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 205005	<b>Status:</b> Ongoing
<b>Title:</b> The Distribution of Bishop Scores and Quantitative Values of Fetal Fibronectin (fFN) in Nulliparous Patients Between 37-42 Weeks Gestation: A Prospective Observational Study			
<b>Principal Investigator:</b> CPT Alison L. Lattu, MC			
<b>Department:</b> OB/GYN		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Bobby C. Howard, MC, USAF; COL Peter G. Napolitano, MC; COL Peter E. Nielsen, MC; MAJ Shad H. Deering, MC; Kathleen T. Gardner, RN			
<b>Start - Completion:</b> 11 Mar 2005 - Feb 2006		<b>Funding:</b> Adeza Biomedical Corp via Geneva Foundation	<b>Periodic Review:</b> 23 Oct 2007

**Study Objective:** To evaluate the distribution of Bishop scores and quantitative values of fetal fibronectin (fFN) in nulliparous patients between the ages 18 - 40 and between 37 weeks through 42 weeks gestation. The secondary objective is to estimate the predictive value of Bishop scores and fetal fibronectin (fFN) testing in predicting delivery outcome (e.g. vaginal or cesarean delivery) in nulliparous patients between 37 weeks through 42 weeks gestation. The third objective is to compare the concordance and statistical agreement between matched fFN test results collected with a speculum and fFN tests results collected without a speculum. In this pilot study sample size is not necessarily sufficient for conclusive results.

**Technical Approach:** This is a prospective observational clinical study in women between the ages of 18 through 40. Between 37 weeks through 42 weeks gestation and following verification of inclusion criteria, fFN testing of cervicovaginal specimen obtained from the lower one-third of the vagina, fFN testing of a cervicovaginal specimen obtained with a speculum and digital cervical exam for the evaluation of Bishop score at the time of their routine prenatal visit. All patients meeting inclusion criteria and who consent to participation will have the following information recorded: patient's age, gestational age, dating criteria, presentation (and how this was assessed), fetal fibronectin test results, Bishop score (specifically, cervical dilation, effacement, station, position, and consistency), and whether or not membrane sweeping was performed. Information will be obtained regarding the most recent time of intercourse and cervical exam. Following delivery, the following information about the patient will be obtained: gestational age at time of admission for delivery, Bishop score (cervical dilation, station, effacement, position, and consistency) at time of admission, indication for admission, whether labor onset was spontaneous, induced, or augmented, length of hospital stay, time from admission to delivery, mode of delivery and birth weight. Additionally, data regarding the presence of the following maternal and fetal complications will be collected: fetal macrosomia (birth weight >4000gm), pre-eclampsia, chorioamnionitis, endomyometritis, meconium stained amniotic fluid, NICU admission, and intrauterine fetal death.

**Progress:** This protocol closed enrollment with a total of 197 subjects enrolled, 30 during FY07. All study related follow-up is complete. The protocol remains ongoing for data analysis.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207069	<b>Status:</b> Ongoing
<b>Title:</b> Resident Self-Assessment in Breast Examination Training		
<b>Principal Investigator:</b> CPT Alison L. Lattu, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Shad H. Deering, MC; LTC Michael K. Chinn, MC		
<b>Start - Completion:</b> 27 Feb 2007 - Apr 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to evaluate the use of a simulation-based training program on resident comfort and proficiency with clinical breast examination.

**Technical Approach:** Residents performed a self-assessment of their exam skills and perceived benefits of the training. The self-assessment was performed before and after the standardized training. Resident performance was assessed during the training and immediate feedback was provided to correct any deficiencies noted during the training. If evaluation of the resident surveys demonstrates the training was, overall, felt to be beneficial, it can be incorporated into our current simulation curriculum.

In addition, findings will be submitted for presentation at the Annual American Professors of Gynecology and Obstetrics conference. Investigators hope to not only demonstrate that Madigan Army Medical Center remains on the leading edge of gynecologic simulation, but also provide other training facilities with a useful and validated simulation tool.

**Progress:** This minimal risk protocol was initially approved by the Expedited Review Committee on 27 February 2007. Protocol documents were released to the PI on 17 August 2007. No work was completed on this study during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205089	<b>Status:</b> Terminated
<b>Title:</b> Pilot Study of a Novel Cord Blood Collection Technique		
<b>Principal Investigator:</b> CPT Megan M. McPhee, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; LTC David E. McCune, MC; COL Peter G. Napolitano, MC; COL Jerome B. Myers, MC; CPT Mitchel T. Holm, MC; CPT Jeremy P. Celter, MS; Carol D. Dean, MPH, BSN		
<b>Start - Completion:</b> 26 May 2005 - Apr 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 22 May 2006

**Study Objective:** Primary Objective: To demonstrate the feasibility of a novel technique for umbilical cord blood collection after delivery. Secondary Objective: To compare this method of collection to historical results obtained from medical literature.

**Technical Approach:** After collecting umbilical cord blood via the method proposed in this protocol, investigators will compare blood volumes and the number of hematopoietic progenitor cells harvested to historical controls. Investigators propose that this new method of cord blood collection after delivery will allow collection of a larger volume of umbilical cord blood than the currently used standard method of cord blood collection thus allowing harvest of a larger number of stem cells. Development of a collection technique which would give a higher yield of stem cells would broaden the range of transplant options available for adult recipients.

**Progress:** This protocol was reported terminated due to lack of interest in continuing this research by the investigators. No work was accomplished on this protocol during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203001	<b>Status:</b> Ongoing
<b>Title:</b> The Effect of Magnesium on Matrix Metalloproteinase-9 Activity in Umbilical Cord Blood at Delivery of Pregnancies Complicated by Chorioamnionitis		
<b>Principal Investigator:</b> COL Peter G. Napolitano, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Patrick M. McNutt, MS; Lisa M. Pierce, D.Sc.; MAJ Christine M. Kovac, MC; LTC Bobby C. Howard, MC, USAF; MAJ Brian T. Pierce, MC; LTC Nathan J. Hoeldtke, MC		
<b>Start - Completion:</b> 8 Oct 2002 - Dec 2002	<b>Funding:</b> DCI	<b>Periodic Review:</b> 4 Oct 2007

**Study Objective:** To determine baseline umbilical cord serum levels of matrix metalloproteinase-9 levels at delivery in pregnancies where labor is complicated by chorioamnionitis compared to normal term controls. To determine if magnesium will reduce the enzymatic activity of serum matrix metalloproteinase-9 in the umbilical cord plasma of neonates from pregnancies complicated by chorioamnionitis compared to normal controls.

**Technical Approach:** Matrix metalloproteinases are zinc-dependent enzymes and it is possible that ionized magnesium which easily crosses the placenta could competitively inhibit MMP-9 enzyme by displacing zinc. We propose to test this hypothesis by first determining what normal levels of MMP-9 enzyme are in pregnancies complicated by infection (those complicated by chorioamnionitis in labor) compared to normal pregnancies with normal labors. Since it would not ethically be acceptable to administer Magnesium sulfate a tocolytic to such complicated pregnancies, we will collect the plasma of such pregnancies then expose it ex vivo to similar levels of magnesium that would be expected if we had treated the mother with standard therapy. Then assay those samples for MMP-9 enzyme activity.

**Progress:** All bench top research has been completed. A paper was submitted but rejected, and the study remains ongoing in case investigators need to collect more specimens, based on peer review of findings.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203045	<b>Status:</b> Ongoing
<b>Title:</b> Randomized Controlled Trial of Endurance Exercise and Gallbladder Disease Risk in Overweight Pregnant Women		
<b>Principal Investigator:</b> COL Peter G. Napolitano, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Peter E. Nielsen, MC; Shirley Beresford, Ph.D; Cynthia Ko, M.D.; Anne McTiernan, M.D.; Deborah J. Bowen, Ph.D; LTC James K. Howden, MC; Sum P. Lee, M.D., Ph.D; Scott J. Schulte, M.D.; Mary Emond, Ph.D		
<b>Start - Completion:</b> 27 Jan 2004 - Jan 2008	<b>Funding:</b> UW via The Geneva Foundation	<b>Periodic Review:</b> 22 Jan 2008

**Study Objective:** (1) To evaluate whether an endurance exercise program is associated with lower risk of gallbladder disease in overweight pregnant women. (2) To evaluate whether an endurance exercise intervention program changes leptin levels in pregnancy among overweight women. (3) To use statistical methods to examine the associations between gallbladder disease incidence and potential causal variables in this prospective trial. These variables include baseline levels of leptin, HDL, insulin levels, BMI (as it varies within women classified as overweight) and changes in these variables. Secondly, we aim to estimate the degree of compliance and overall adherence to an exercise intervention in normal weight pregnant women, in the context of a randomized intervention study.

**Technical Approach:** This trial will evaluate the effect of an intervention designed to increase regular endurance exercise of moderate to vigorous intensity on the risk of gallbladder disease in pregnancy.. Women will be stratified according to overweight or normal weight status. The randomized controlled trial will be confined to the former group (n=862), while a feasibility trial will be conducted among 250 normal weight women. The comparison groups will receive the exercise intervention in the post-partum period. They will continue their usual activities during pregnancy. Thus all women participating in the trial will receive the benefit of exercise training at some point during the study period. The study population will be pregnant women aged 18 to 45. All women presenting for prenatal care will be potentially eligible. Additional clinical procedures specific to the study include a first and third trimester ultrasound of both the gallbladder and the fetus, and an additional blood draw at those times. Usual care includes a second trimester ultrasound of the fetus, to which will be added an ultrasound of the gallbladder, and a blood draw, to which additional tubes will be added. To enhance cooperation with additional study procedures in the exercise intervention study, we will provide a \$30 financial incentive for completing the 1st trimester and late 3rd trimester blood draws. This incentive will not be provided for the early 3rd trimester blood draw, since it occurs at the same time as a routine prenatal blood draw. As an added incentive to participate, an additional scan of the fetus will be made at the first trimester gallbladder ultrasound examination. This will allow women an early glimpse of their baby. For women who have other children, we will provide a reimbursement for childcare expenses (\$3 per hour) during exercise or stretching classes. Pedometers will be provided during the study for the intervention group, and at the postpartum visit for the control women.

**Progress:** As of January 2007, 3,962 women were approached with information about the study, and 988 women agreed to enroll, of which 235 were disqualified because of stones/miscarriage/failure to comply with study requirements/medical conditions. At the time of this report, 531 have completed the study. Expanding the BMI range to 34.9 has enrolled 42 additional women that would not have qualified for the study. Subject recruitment continues.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203099	<b>Status:</b> Ongoing
<b>Title:</b> Umbilical Cord Plasma Homocysteine Concentrations at Delivery in Pregnancies Complicated by Preeclampsia		
<b>Principal Investigator:</b> COL Peter G. Napolitano, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Christopher S. Murphy, MC; CPT Charles L. Wakefield, MC		
<b>Start - Completion:</b> 1 Aug 2003 - Dec 2003	<b>Funding:</b> DCI	<b>Periodic Review:</b> 25 Jun 2007

**Study Objective:** The purpose of this study is to evaluate the level of umbilical cord plasma homocysteine in gestations complicated by pre-eclampsia compared to normotensive gestations.

**Technical Approach:** General Protocol Sampling Umbilical cord blood samples will be obtained immediately after cord clamping by direct venipuncture of the umbilical vein collected in lavender top tubes. The specimens will be stored on ice and centrifuged at 3000 rpm for 15 min as soon as possible. After extracting the serum plasma, it will be divided into several aliquots for storage. All specimens will be frozen and maintained at -70o C. Maternal plasma obtained at the time of routine labor admission blood work will be collected and stored in a similar fashion. At four points during the study, the specimens will be collected and sent to William Beaumont Army Medical Center, TX, Dept of Pathology for homocysteine level analysis. A sample of 1mL of EDTA plasma is necessary for laboratory analysis. The plasma homocysteine level is measured by ADVIA Centaur HCY assay. Each specimen will be run in duplicate.

**Progress:** This protocol remains ongoing. Investigators requested and received approval to recruit a subset of women who are preterm preeclampsia (five), and another (five) who are preterm preeclampsia with IUGR fetuses. Details on specimen analysis are being worked out with the Department of Pathology, as the prior site (WBAMC) no longer does the testing. Specimens will likely be batched and sent to Quest for analysis.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207125	<b>Status:</b> Ongoing
<b>Title:</b> In Vivo Effects of Medroxyprogesterone Acetate on Lipopolysaccharide Induced IL-6 Expression and ERK-Kinase Activity		
<b>Principal Investigator:</b> COL Peter G. Napolitano, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Lisa M. Foglia, MC; CPT Michael J. Hartenstine, MS; Danielle L. Ippolito, PhD; LTC Demetrice L. Hill, MC		
<b>Start - Completion:</b> 25 Sep 2007 - Sep 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this protocol is to evaluate the inflammatory response of maternal peripheral mononuclear cells to exposure to lipopolysaccharide in women before and after receiving depot-medroxyprogesterone acetate.

**Technical Approach:** Peripheral blood will be collected from patients pre- and post-treatment with medroxyprogesterone acetate (Depo-Provera™). Mononuclear cells will be isolated and exposed to lipopolysaccharide. The response of cells will be assessed by measuring ERK-kinase activity and IL-6 production. The levels pre- and post-exposure will be compared.

**Progress:** This minimal risk protocol received final approval by the Expedited Review Committee, effective 25 September 2007.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207102	<b>Status:</b> Ongoing
<b>Title:</b> Prevalence, Risk Factors, and Common Organisms in Urinary Tract Infections in Urogynecologic Patients		
<b>Principal Investigator:</b> CPT Coryell J. Perez, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Jeffery L. Clemons, MC		
<b>Start - Completion:</b> 12 Jun 2007 - 6/08	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objectives of this protocol are to determine the prevalence of Urinary Tract Infection (UTI) in new urogynecology patients, the most common organisms in UTIs in urogynecology patients, and specific urogynecologic risk factors for UTI, for example, anterior vaginal wall prolapse, stress urinary incontinence, overactive bladder, pelvic organ prolapse.

**Technical Approach:** We will review charts of approximately 600 patients who have presented to the Madigan Army Medical Center Urogynecology clinic over the past 2 years. All new patients during this time frame will be included.

Patients were referred for any number of urogynecologic complaints, including pelvic organ prolapse, recurrent urinary tract infections, interstitial cystitis, and incontinence. All patients presenting to the Urogynecology clinic underwent an initial evaluation which included history, physical exam, measurement of prolapse if present, and collection of catheter urine specimen. Some patients also underwent urodynamic testing if urinary incontinence was a concern.

We will collect data onto individual data sheets. The data we collect will include demographic information, pertinent past medical history, results of physical exam and urodynamics testing, and culture results and resistance profile of catheter urine specimen collected during initial evaluation. The data collection sheets will be compiled into a spreadsheet.

We will calculate the prevalence of urinary tract infection among all new patients presenting to the urogynecology clinic during the study review period. We will also calculate odds ratios to look for statistically significant risk factors for urinary tract infections. Specifically, we have powered our study to evaluate anterior vaginal wall prolapse as a risk factor for urinary tract infection.

**Progress:** Approximately 150 charts have been reviewed during FY 2007, with a continuing plan to review approximately 600 charts. Analysis of the data has not begun.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207083	<b>Status:</b> Completed
<b>Title:</b> Operation Enduring Freedom: Trends in Combat Casualty Care by Forward Surgical Teams Deployed to Afghanistan		
<b>Principal Investigator:</b> LTC Jane Shen-Gunther, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 13 Apr 2007 - Sep 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to examine the clinical experience of the U.S. Army 759th Forward Surgical Team (FST) deployed to Afghanistan between December 2005 and November 2006, and compare these data with those of three published reports from previously deployed FST between years 2001-2003.

**Technical Approach:** During deployment, clinical data on all combat casualties and surgical consults evaluated by the FST were recorded and data entered in an electronic database. Data includes age, gender, military affiliation, and national origin, and trauma characteristics with respect to the following variables: mechanism of injury; anatomical location, type and severity of injury; blood product utilization; and surgical procedures performed. Data on non-combat trauma and non-trauma cases were also maintained. Main outcome measures to include mechanism of injury, injury distribution, injury severity wound characteristics, and types of surgical procedures will be summarized by descriptive statistical methods. Comparison of outcome measures with those of historical studies will be analyzed using the Chi-square test for non-parametric variables.

**Progress:** This protocol was reported completed in July 2007, and an abstract submitted for publication clearance; however Operational Security disapproved results being published. A copy of the abstract is on file in DCI.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205021	<b>Status:</b> Completed
<b>Title:</b> Correlation of Persistent Anal Sphincter Defects and Symptoms following Repair of Anal Sphincter Lacerations due to Obstetric Injury in Primiparous Women		
<b>Principal Investigator:</b> CPT Christine M. Vaccaro, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Jeffery L. Clemons, MC; CPT Rhiana D. Saunders, MC		
<b>Start - Completion:</b> 10 Dec 2004 - Jan 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 21 Nov 2006

**Study Objective:** To identify the incidence of persistent anal sphincter defects following repair of anal sphincter lacerations (ASL) due to obstetric injury in primiparous women. To correlate the size of the persistent anal sphincter defect (ASD) with anal incontinence symptoms. To identify the size of ASD at which symptoms increase dramatically, if any. To identify risk factors for symptomatic ASD.

**Technical Approach:** A prospective observational study will be conducted over a 24 month period. Primiparous women that have sustained an ASL and undergone successful repair will be recruited during their postpartum stay at MAMC. Obstetric records will be reviewed to collect demographic data, medical history, delivery outcomes, and anal sphincter repair technique. At 8 weeks postpartum, each woman will undergo endoanal sonography and complete the Wexner anal incontinence questionnaire. The endoanal ultrasound will be used to detect and measure the size of ASD. A persistent ASD will be defined as any defect of the integrity of the IAS or EAS. Photographic images will be taken of the largest portion of the ASD. The size of the defect (in degrees) will be measured by a protractor. The length of the defect (in millimeters) will be measured by 3-D ultrasound. Three researchers will perform all measurements. The endosonographer will be blinded to the questionnaire results. The Wexner anal incontinence questionnaire assesses the presence and frequency of incontinence to flatus, liquid and solid stool, pad use, and lifestyle alteration. Scores can range from 0 (complete continence) to 20 (severe incontinence to solid stool on a daily basis). A score of 4 or more at 2 months post-partum will define a symptomatic ASD. Women with and without symptomatic ASD will be compared to identify risk factors for symptomatic ASD. Approximately 72 women with ASD will be needed to demonstrate a difference in defect size between symptomatic and asymptomatic ASD. Demographic and delivery data will be entered onto a Data Sheet. The ultrasound data and questionnaire data will be also entered onto the Data Sheet. All data will then be transferred to the Excel spreadsheet. Security issues will be enforced (locking computer and office).

**Progress:** This protocol was reported as completed during FY07. A total of 47 subjects enrolled in the study during FY 2005-2006, and follow-up was conducted through October 2006. A manuscript is in submission for publication, and the study was awarded the "Resident Research Award" by the American College of Obstetrics and Gynecology in October 2006.

**Results:** The incidence of anal incontinence symptoms at 8-12 weeks was 43%, and 21% of women reported a negative effect on their quality of life. The incidence of anal sphincter defects was 79%, with IAS defects found in 32% and EAS defects found in 77%. IAS defects > 45 degrees were predictive of anal incontinence symptoms (odds ratio 6.7, 95% CI 1.2, 37.3, p=.02), but EAS defect size was not associated with symptoms (p=.91). After 12-24 months, 8.5% reported chronic anal incontinence symptoms.

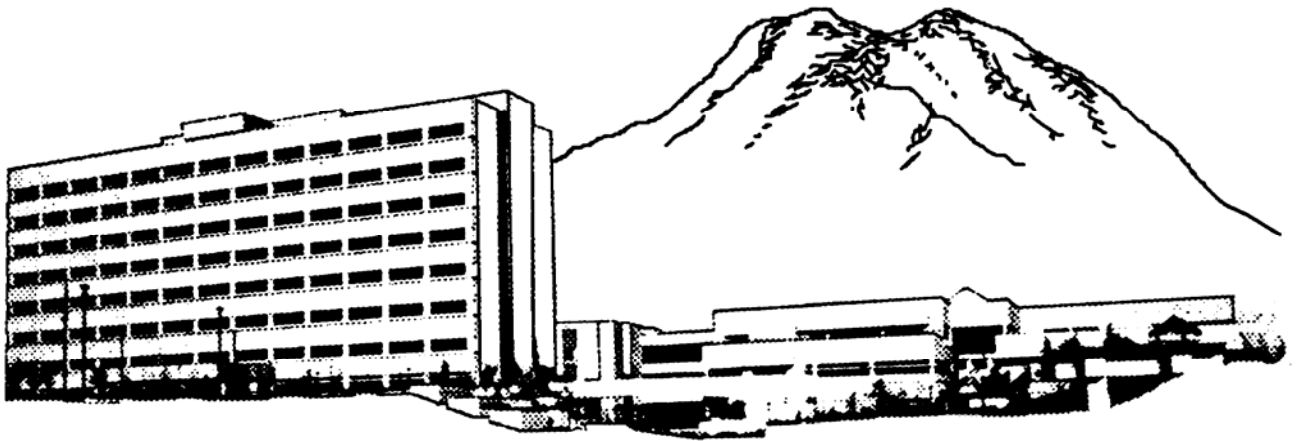
### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207085	<b>Status:</b> Ongoing
<b>Title:</b> Simulation Training to Evaluate the Force Used During Vaginal Delivery and Shoulder Dystocia		
<b>Principal Investigator:</b> CPT Leslie L. Weeks, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Shad H. Deering, MC; Karen A. Winter, DAC		
<b>Start - Completion:</b> 24 Apr 2007 - Apr 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to have residents and staff from the departments of OB/GYN and Family Medicine and L&D nurses engage in a simulated shoulder dystocia scenario to evaluate how much force different types of providers apply to the infant head during routine deliveries as compared to those complicated by shoulder dystocia.

**Technical Approach:** Staff, Midwives, Labor and Delivery Nurses and Residents from Family Medicine and Obstetrics & Gynecology will be asked to perform a simulated delivery on a birthing simulator with a force-feedback monitor attached. After the delivery, which will include description of a shoulder dystocia, feedback will be given as to how much force was applied during the delivery. Analysis will be performed to determine how practice specialty, level of training, personal experience, gender, and body habitus all influence the amount of force a particular provider will apply to the infant head during a normal delivery, a shoulder dystocia, and a shoulder dystocia during which routine methods of resolution have failed. Although there is no definitive answer to the amount of force that is "too much," this study will perhaps allow physicians to begin to estimate that number and provide feedback to those participating on how much force was applied during delivery.

**Progress:** This minimal risk protocol was approved by the Expedited Review Committee on 24 April 2007. A total of 74 providers consented to participate in this study thus far. All completed participation and the program is continuing.



# **Detail Summary Sheets**

Department of Pathology

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205042	<b>Status:</b> Completed
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**Title:** Incidental Anatomic and Histologic Findings in Bariatric Surgery Specimens

**Principal Investigator:** MAJ Anne L. Champeaux, MC

**Department:** Pathology

**Facility:** MAMC

**Associate Investigator(s):** MAJ James B. Branch, MC; CPT Vance Y. Sohn, MC

**Start - Completion:**

14 Feb 2005 - Apr 2005

**Funding:**

DCI

**Periodic Review:**

30 Jan 2007

**Study Objective:** Collection, review and compilation of anatomic/histologic findings in bariatric surgery specimens processed by Madigan Army Medical Center (MAMC) Department of Pathology, Anatomic Pathology Service from 1994-2004.

**Technical Approach:** Collection, review and analysis of bariatric surgery specimen reports generated by the MAMC Anatomic Pathology service from 1994 through 2004 to identify and correlate anatomic and histologic findings with age and gender. The study aims to elucidate the range of anatomic and histologic variables found in partial gastrectomy, gallbladder and appendices removed during bariatric procedures.

**Progress:** This protocol was completed during FY 2007. Results: Abnormal findings were divided based on the organ. In the gastric remnant, reported pathology included: 66 gastritis, 7 fundic gland polyps, 3 intestinal metaplasia, 2 gastric ulcers, 2 reactive gastropathy, 1 lymphoid aggregate, 1 diverticulum, 1 developmental cyst, and 1 leiomyoma. 311 appendixes were analyzed with the following abnormalities: 76 fibrous obliteration of the appendiceal lumen, 2 carcinoids, 2 infarcted appendiceal epiploica, 2 follicular hyperplasia, and 1 subserosal endometriosis. In the gallbladder the sole abnormality, other than cholelithiasis, was an adenomyoma. Other resected findings included five Meckel's diverticula, one bile duct adenoma, and one sigmoid diverticulum.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205102	<b>Status:</b> Completed
<b>Title:</b> Absolute Lymphocytosis in Adults: A Laboratory Protocol		
<b>Principal Investigator:</b> CPT Colby A. Fernelius, MS		
<b>Department:</b> Pathology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Daniel L Cruser, MC; LTC Dale L. Waldner, MS; CPT Mitchel T. Holm, MC; COL Jerome B. Myers, MC; CPT Jared M. Andrews, MC		
<b>Start - Completion:</b> 12 Jul 2005 - Oct 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 12 Jun 2006

**Study Objective:** The objective is to analyze and report correlations between diagnosis rendered by flow cytometry analysis of patients with peripheral blood lymphocytosis, and the lymphocyte counts and other demographics of the patients. International guidelines for flow cytometric analysis of peripheral blood lymphocytosis to rule out leukemia/ lymphoma are not well defined. These correlations can be used to help develop hospital protocols for the evaluation of absolute lymphocytosis in adults.

**Technical Approach:** This is a retrospective, descriptive study of Madigan Army Medical Center's process for analysis of peripheral blood lymphocytosis in persons greater than 18 years of age. By analyzing the demographic data, CBC, and flow cytometrical results obtained, it is our hypothesis that this information can be beneficial in more accurately defining guidelines for the use of flow cytometry for lymphocytosis, and promote further prospective research in this area.

**Progress:** This protocol was completed in June 2007, and an abstract submitted for publication.

**Results:** Approximately 7,300 CBC specimens/month (3,400 from patients  $\geq 50$  years of age) were performed. Of these, an average of 44 specimens/month had a lymphocytosis of  $\geq 4E+9$  Cells/L, from approximately 28 different patients. From this group 71 flow cytometric cases (an average of 2/month) were performed over the 2 year period. 42 cases (59%) had an abnormal phenotype. 27 had a phenotype consistent with CLL, and the other 15 were a mixture of LPDs involving B and T -lymphocytes as well as NK cells. Comparing normal phenotype to abnormal phenotype showed statistically significant differences between the mean age (n-60.4 +/- 7.5, abn-69.8 +/- 8.7), ALC (n-4.9 +/- 0.8, abn-9.2 +/- 8.1), and relative lymphocyte count (RLC) (n-43.9 +/- 7.5%, abn-59.3 +/- 8.8%).

**Conclusion:** Absolute lymphocyte counts  $\sim 4E+9$  Cells/L in adults  $\sim 50$  years of age represent approximately 1% of the CBCs performed in our laboratory. Review of these cases by a pathologist is logistically feasible due to the low incidence. Our method of reviewing for morphology, clinical history, and past lymphocyte counts with comments to the ordering clinician yielded a high incidence of abnormal phenotype diagnoses when evaluated by flow cytometric analysis (59%). Age, ALC, and relative lymphocyte counts are variables that can be used to develop guidelines for determining the appropriateness of flow cytometric analysis. Patients less than 52.4 years of age fall below two standards of deviation from the mean age of the abnormal phenotype group. The standard of deviation for mean ALC is very small (4.9 +/- 0.8), which indicates that counts greater than two standards of deviation above the mean, or  $6.5 E+9$  Cells/L, would correlate strongly with an abnormal phenotype. The same conclusion could be made with a RLC greater than 58.9%. In conclusion, patients greater than or equal to 50 years of age with an ALC greater than  $6.5E+9$  Cells/L or a RLC greater than 58.9% are likely to have a lymphoproliferative disorder and flow cytometric analysis is indicated.

### Detail Summary Sheet

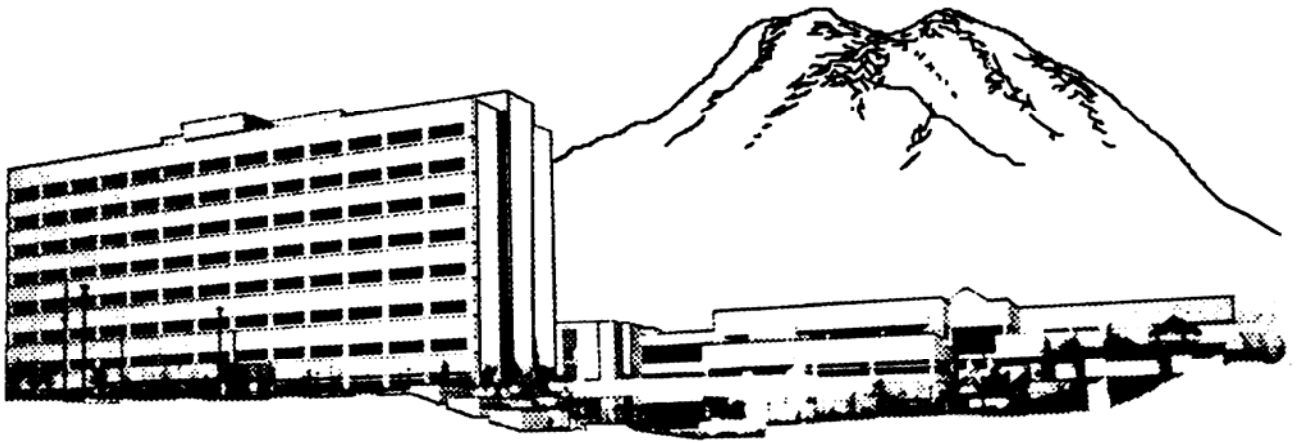
<b>Date:</b> 30 Sep 07	<b>Number:</b> 203041	<b>Status:</b> Ongoing
<b>Title:</b> Use of a Non-FDA Approved Gene Amplification Test To Detect or Rule-Out Vaccinia in Patients With Complications Following Smallpox Vaccination or Possible Contact Vaccinia		
<b>Principal Investigator:</b> LTC Helen B. Viscount, MC		
<b>Department:</b> Pathology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Edward P. Ager, MS; MAJ Steven D. Mahlen, MS; COL Joseph T. Morris III, MC; COL (Ret) Mary P. Fairchok, MD; COL Peter G. Napolitano, MC		
<b>Start - Completion:</b> 30 Apr 2003 - Mar 2004	<b>Funding:</b> DCI	<b>Periodic Review:</b> 22 Jan 2008

**Study Objective:** To determine the sensitivity, specificity and clinical utility of the only test currently available to detect vaccinia virus in patients who may be experiencing post-vaccination complications following smallpox vaccination, or in close contacts of vaccinees who may have been inadvertently inoculated with the vaccinia virus (contact vaccinia).

**Technical Approach:** Clinicians seeing patients with possible post-vaccination complications or suspected contact vaccinia will collect and submit three swabs of lesion fluid to one of the DOD Confirmatory Labs with the vaccinia test. One swab will be used for vaccinia PCR using either the Cepheid SmartCycler or the Idaho Technology LightCycler platforms that are approved as LRN tools. DNA extraction and amplification will be done strictly following the LRN protocol. Extraction of DNA from exudate material and specimen processing will take approximately 2 hours. Amplification results will be final approximately 30 minutes after the amplification begins. A positive amplification result is determined by standardized parameters and with a calculated threshold done by the real-time PCR unit. The second swab will be used for viral culture. Vaccinia virus produces cytopathic effects (CPE) in most common cell lines used in clinical virology labs. The CPE resemble those of HSV, CMV and adenovirus. While clinical labs can rapidly identify HSV, adenovirus and CMV in infected cell lines using DFA, there is no such test for vaccinia. However, if a specimen results in CPE, but is negative for HSV, adenovirus and CMV by DFA, then that culture may be a presumptive result for vaccinia, and will be result as "CPE from lesion material - negative for HSV, adenovirus, and CMV". Specimens with no resultant CPE will be finalized as "No virus detected". The third swab will be submitted for bacterial culture and sensitivity (standard of care). Viral and bacterial culture data, along with PCR data will be used in conjunction with the clinical situation to help determine if the patient has post-vaccinial complications due to vaccinia virus, contact vaccinia, or is experiencing rashes or lesions due to other causes. All specimens kept at the DOD LRN Confirmatory Labs will be handled and disposed of in accordance with federal regulations.

**Progress:** This "CDC" protocol remains open to enrollment with six subjects enrolled since study approval, none during FY07. No changes to the protocol were reported, although a change in the role of principal investigator from MAJ Ager to LTC Viscount was submitted and approved.





# **Detail Summary Sheets**

## Department of Pediatrics

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207124	<b>Status:</b> Ongoing
<b>Title:</b> Safe Minimum Wrestling Weights: How Familiar are Health Care Providers with Means of Determining Safe Weights, and are Current Guidelines Practical in the Typical Outpatient Clinic Setting?		
<b>Principal Investigator:</b> CPT Jesse J. Barondeau, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Franklin H. Wood, MC		
<b>Start - Completion:</b> 24 Sep 2007 -	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine the percentage of health care providers who see wrestlers for pre-participation physical exams who are knowledgeable and/or comfortable in properly determining a safe minimal weight. Consequently, this may reveal that a more practical recommendation for determining safe minimal weight requirements for wrestlers is needed.

**Technical Approach:** Primary care givers to include Pediatricians, Family Medicine physicians, Physician's Assistants, and Nurse Practitioners who perform pre-participation physicals with minimal wrestling weight allowances in their practices will be included in the data. We would like to receive at least 180 responses from both civilian and military providers via an email survey. The data will be divided into the different specialties listed as above and by years of experience. The variables will include levels of comfort in determining minimum allowable wrestling weights, familiarity and training experience with different techniques for assessing safe minimal wrestling weights, amount of time spent counseling on nutrition and weight concerns with these select patient encounters, and opinion on care givers level of influence on these patients. This data will be formulated into percentages and then comparisons will be made between the different groups and as a whole.

**Progress:** This minimal risk protocol received final approval by the Expedited Review Committee, effective 24 September 2007.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207025	<b>Status:</b> Ongoing
<b>Title:</b> Measuring Professionalism in Pediatric Residents: Feedback on Patient Encounter Videotaping		
<b>Principal Investigator:</b> LTC Victoria W. Cartwright, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> None.; LTC Amy B. Connors, MC		
<b>Start - Completion:</b> 11 Dec 2006 - Jun 2009	<b>Funding:</b> DCI	<b>Periodic Review:</b> 26 Nov 2007

**Study Objective:** The objectives of this study are to (1) measure residents' performance of professionalism in real-time clinical care, (2) validate a tool that is useful for measuring professionalism and communication skills in the pediatric setting, and (3) measure improvement of resident professionalism, both over time during their residency training as well as after instituting a curriculum concerning professionalism and communication.

**Technical Approach:** This project has several parts: use a new tool devised by faculty consensus, called the videotaping precepting form, in the already established videotaping portion of the pediatric outpatient clinic. The videotaping occurs at least once a year for each resident, therefore measuring their professionalism and communication during their PL-1, PL-2 and PL-3 years; Validate this new tool by having several different raters use the tool on the same videotaping session; compare the PL-1, PL-2 and PL-3 residents' performance with this tool and institute a "communication and professionalism" curriculum and measure pre- and post-curriculum residents' performance.

**Progress:** This minimal risk protocol was approved by the Expedited Review Committee 11 December 2007. Investigators continue to collect data on each residency year group of residents while they are videotaped in the outpatient pediatric clinic setting. Curriculum implementation has not begun; therefore, post-curriculum measurements for comparison have not been initiated. Some preliminary data information has been collated in a descriptive format as an abstract submission to the Uniformed Services Pediatric Seminar, March 2008 (have not yet heard back if this will be accepted for presentation). After December 2007, a change in the role of PI will be submitted so that LTC Amy Connors may be the future point of contact.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204074	<b>Status:</b> Completed
<b>Title:</b> Survey of Chronic Pain and Its Effects on Youth With Disabilities		
<b>Principal Investigator:</b> COL Beth E. Davis, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Joyce M. Engel, PhD, OTR/L; Kenneth M. Jaffe, M.D.; John F. McLaughlin; Mark P. Jensen, PhD; Dawn Ehde, PhD		
<b>Start - Completion:</b> 16 Jun 2004 - May 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 10 Aug 2006

**Study Objective:** This study has two specific aims: (1) to increase our understanding of the frequency and severity of pain problems in youth with spina bifida (SB), muscular dystrophy (MD), cerebral palsy (CP), limb deficiency (LD), and spinal cord injury (SCI); and (2) to develop a biopsychosocial model for the study of chronic pain in youth with disabilities.

**Technical Approach:** This study uses a cross sectional design. A convenience sample of 100-150 youths will be interviewed in-person or over the telephone to complete a standardized questionnaire on pain. The youths' parent/guardian will also be invited to complete a questionnaire (assistance will be provided as needed). Subject inclusion criteria include: a primary diagnosis of CP, LD, SCI, SB, or MD, a chronological age range of 8-to-20 years, capacity for expressive communication which may include the use of augmentative communication devices, English as the primary language, and no more than mild cognitive impairment. Subjects will be paid \$40.00 (\$25.00 for youth and \$15.00 for parent/guardian) for the completion of interview/questionnaire. Potential subjects will first be contacted directly by Dr. Beth Ellen Davis or medical personnel involved in the care of the youths, via an approach letter mailed by Dr. Davis, or posting of a recruitment flyer. Parents/guardians and young adults who are interested in the study will be asked to return an interest/information form in the provided postage-paid envelope to Dr. Davis at the Developmental Pediatrics Clinic at Madigan Army Medical Center. Dr. Davis will then inform UW investigators via confidential e-mail, a letter sent through the mail or telephone calls of those families interested in participating. UW research personnel will then contact these potential subjects. Interested parents/guardians or youth may also contact the principal investigator or study project director via e-mail or telephone. At the time of the contact, the purpose and procedures of the study will be explained and the parent/guardian will have the opportunity to ask questions. If the parent/guardian and youth express interest in the participating in the study, the investigator will screen to insure that all inclusion criteria have been met including a brief cognitive screening. If the inclusion criteria are met, an interview will be scheduled at a time and place (University of Washington Medical Center, the subject's home, or over the telephone for youths without speech difficulties) that is most convenient for the subjects. Assent and consent forms will be completed by the youth and parent/guardian prior to the initiation of the interview/questionnaire. A brief, standardized cognitive screening will also be completed prior to initiation of the interview (youth subject must score a minimum of 17/25 on the modified Mini Mental Status Examination to be eligible for participation. A subject descriptive information sheet will be completed. The youth will then be interviewed in-person or over the telephone by a study investigator or trained research assistant while the parent/guardian completes a disability specific form and a written questionnaire. The youth's interview and parent/guardian questionnaire each will take approximately 10 to 50 minutes to complete depending on whether or not the youth reports recurrent, bothersome pain. Response keys are used throughout the interviews to facilitate answering questions. All data will be entered into MS ACCESS. After all data have been entered, variables will be inspected for outliers and skewness and adjusted using appropriate transformations. Descriptive analysis will then be performed.

**Progress:** This protocol was reported as completed in December 2007. Subgroups of youth with spina bifida (30), cerebral palsy (57), and muscular disorders (20) in the study from other sites have been identified and initial descriptive data analyzed. Abstract for pain in youth with spina bifida was submitted and accepted for poster presentation at the American Academy for Cerebral Palsy and Developmental Medicine, September 14-17 2005, Orlando, FL.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 204104	<b>Status:</b> Completed
<b>Title:</b> Health, Quality of Life & Activity in Cerebral Palsy			
<b>Principal Investigator:</b> COL Beth E. Davis, MC			
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert L. Miller, MC; Kristie Bjornson, PhC, PT			
<b>Start - Completion:</b> 13 Sep 2004 - Jun 2006	<b>Funding:</b> United Cerebral Palsy Research & Education Foundation via Grant		<b>Periodic Review:</b> 10 Aug 2006

**Study Objective:** Aim 1. To test for differences in activity performance, self and parent reported health status and QOL (Quality Of Life) among youth with CP (Cerebral Palsy) and TDY (Typically Developing Youth) by level of activity capacity, while controlling for baseline activity performance and capacity, age, gender, SES and current day outlook. The predicted differences in activity performance, self-reported health status will be such that TDY will be greater than CP youth (TDY > CP), and that these differences will be ordered by defined levels of activity capacity with the Gross Motor Function Classification System (GMFCS) such that TDY > Level I > Level II > Level III, while controlling for baseline activity performance, age, gender, SES and current day outlook. The predicted differences in QOL will not be ordered by activity capacity.

Aim 2. To examine the associations between activity level (performance) and self and parent perceived health status and QOL in youth with CP and TDY, while controlling for baseline activity performance and capacity, age, gender, SES and current day outlook. There will be a positive linear relationship by activity capacity level (GMFCS) between activity performance and the health status physical domain (Child Health Questionnaire, CHQ-P). There will be a positive linear relationship by activity capacity (GMFCS) between activity performance and the QOL relationship domain (Youth Quality of Life, YQOL-R). The relationship of activity performance to the health status psychosocial domain (CHQ-PS) and the QOL self, environment and general QOL (YQOL-R: S, E & GQOL) will not be linear by activity capacity level.

Aim 3. Explore a model specifying the influence of activity capacity and activity performance on health status and quality of life controlling for baseline activity performance, age, gender, SES, and current day outlook.

**Technical Approach:** This is a multi-center study that intends to study the health, quality of life, and activity in children with cerebral palsy. Children with the diagnosis of cerebral palsy, Gross Motor Function Classification System (GMFCS) levels I-III and typically developing youth, ages 10 to < 14 years, with the ability to read and understand at the 10 year age level will be studied. 30 children with cerebral palsy and 10 children that are typically developing that meet inclusion criteria through the MAMC study site will be enrolled, as well as one parent/guardian of each child enrolled (40 parents). Potential study participants will be recruited through a focused direct mailing of an approach letter introducing the project to the guardians of children with CP and typically developing youth that have had medical care at the MAMC Developmental Pediatrics, General Pediatrics, and Family Practice clinics. An informational letter will be sent to school based nurses, physical and occupational therapists, or other health care providers at military facilities in Western Washington. The letter will introduce the project, state that ambulatory children with CP and TDY are being sought for participation in the study, the inclusion criteria and brief description of the project. Local health care providers can then approach their patients about interest in the study and give them the contact information of the PI and/or contact the PI for further information about the project.

Once consent and assent have been attained, there will be two research visits seven days apart in

the participants' home at their convenience. At the first visit, the youth will be asked to complete the questionnaires and have the Step Watch calibrated to their walking pattern. They will be asked to wear the Step Watch for seven days. On day seven, researchers will return to their home to download the information from the Step Watch and complete appropriate questionnaires. Parents/ guardians will be asked to complete the appropriate questionnaires on visit day one and visit day seven. For specific primary and secondary outcomes, design and procedures, data preparation, and analysis, see sections 9.3 through 9.6 in the Master Protocol.

**Progress:** This protocol was reported as completed in December 2007. Data collection was completed for twenty MAMC subjects, sixteen during FY06. Data collection continued for subjects in specific categories of impairment related to their CP from the CHRMC research office, for a total of over 100 patients with cerebral palsy. This was completed in December 2005. Data analysis began and Principal PI at CHRMC (K. Bjornson) defended PhD dissertation with results. Initial manuscript preparation underway regarding the scope of activity recorded for varying degrees of physical impairment in children with cerebral palsy.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206049	<b>Status:</b> Ongoing
<b>Title:</b> An Observational Study to Determine the Factors Influencing Bone Mineral Density in Post-Menarchal Adolescents with Neuromuscular Disabilities		
<b>Principal Investigator:</b> MAJ Michelle K. Ervin, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Beth E. Davis, MC; COL Stephen M. Yoest, MC; COL (Ret) Patrick C. Kelly, D.O.; LTC Antonio G. Balingit, MC		
<b>Start - Completion:</b> 7 Mar 2006 - Jun 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 27 Feb 2007

**Study Objective:** To determine bone mineral density measurements by use of DEXA technique at the distal femur, in a heterogeneous group of post-menarchal females with neuromuscular disabilities and compare to previously published reference data of age-matched normal controls. To describe the associations between bone mineral density measurement and multivariate factors such as: 1) anti-epileptic medication use, (2) mobility status as defined by the Gross Motor Function Classification System (GMFCS; see appendix for description of this scale), (3) Body mass index (BMI), (4) Tanner staging, and (5) hormonal contraceptive use while controlling for nutritional intake, specifically calcium and vitamin D.

**Technical Approach:** This observational pilot study will evaluate the bone mineral density in a heterogeneous group of 45 post-menarchal females ages 11 through 24 with neuromuscular disabilities that meet the inclusion criteria. The change in bone mineral density will be descriptively compared. Potential subjects will be recruited through a focused direct mailing of an approach letter introducing the project to the subject and/or guardians of eligible adolescent females receiving care at the Madigan Army Medical Center Pediatric Clinic, Adolescent Clinic, and Developmental-Behavioral Clinic. The letter will introduce the project, and state that post-menarchal females with neuromuscular disabilities are being sought for participation in the study, the inclusion criteria and a brief description of the project. Once consent, assent or surrogate consent has been obtained, a clinic appointment will be scheduled with a member of the investigative team to conduct an intake history and physical exam, and initiate dietary assessment through the use of a three day diet diary. Those participants identified as having insufficient calcium and/or vitamin D intake will be provided with supplemental therapy. Subjects will have distal femur bone mineral density measured at baseline, 6 months and 12 months. No current reference normative data exists for this population. Once all of the data is collected BMD measurements will be descriptively compared using multivariate logistical regression to determine significance of osteopenia risk factors identified for each subject.

**Progress:** This protocol remains ongoing for continued data collection and analysis.

**INTERMEDIATE RESULTS:** 18 subjects have been screened. Their z scores ranged from -4.5 to 1.5. Nearly all of the subjects have negative z scores. Exposure to chronic anti-epileptic medication (AED) was associated with lower z scores. Co-existence of AED and depot medroxyprogesterone acetate (for menstrual control) was associated with the lowest z scores amongst the group (range -4.5 to -3.6). Ambulatory status was not found to be a significant factor in BMD of the lumbar spine.

**CONCLUSIONS:** This survey of BMD in post-menarchal adolescent girls with neuromuscular disabilities suggests a high prevalence of LBMD in this group of patients. Chronic AED exposure and depot medroxyprogesterone acetate appear to be important risk factors for LBMD.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205138	<b>Status:</b> Completed
<b>Title:</b> Evaluation of Serologic Responses to Fluzone® in Infants > 6 Months of Age Who Did or Did Not Receive Fluzone Vaccine at 2 Months of Age		
<b>Principal Investigator:</b> COL (Ret) Mary P. Fairchok, MD		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Sue E. Chambers, RN		
<b>Start - Completion:</b> 17 Nov 2005 - Sep 2006	<b>Funding:</b> Sanofi Pasteur via The Geneva Foundation	<b>Periodic Review:</b> 26 Sep 2006
<p><b>Study Objective:</b> To demonstrate the safety and immunogenicity of Fluzone vaccine administered in 6 month olds who have previously received this immunization compared to 6 month olds who have not received this vaccine previously.</p> <p><b>Technical Approach:</b> This is an observational and descriptive study that will provide preliminary comparative information about the safety and immunogenicity of Fluzone vaccine among children who were given Fluzone vaccine at 2 months of age as part of MAMC protocol 205034 (Group 1) versus children who have never received influenza vaccine (Group 2). All participants will be enrolled after obtaining informed consent from their parent or guardian.</p> <p>At study visit 1, all participants will undergo informed consent, and a medical history and directed physical exam will be conducted. All participants will then receive one 0.25 mL intramuscular injection of Fluzone®. Both groups will be provided with a diary card to take home at this visit, recording solicited and unsolicited local and systemic adverse effects of the vaccines as well as daily temperatures for the 7 days after the visit.</p> <p>At study visit 2, a blood sample will be collected from all subjects, and both groups will receive a second 0.25ml intramuscular injection of Fluzone®. Interim histories and diary cards will be collected and a second diary card will be provided.</p> <p>At study visit 3, a blood sample will be collected from all subjects. Diary cards and interim history will be obtained. There will be a follow up contact by phone of all study participants at 6 months after visit the last dose of Fluzone® to solicit adverse events.</p> <p>Other, non-study, vaccinations may be given at any study visit or at any time beginning 15 days following Visit 2. No vaccinations may be given between Visit 1 and Visit 2, nor in the 14 days preceding Visit 1 or following Visit 2.</p> <p>Outcome variables for safety include 1. Frequency and percentage of subjects who had solicited injection site and systemic reactions 2. Frequency of subjects reporting medically attended unsolicited adverse events and serious adverse events and the frequencies of these events</p> <p>Outcome variables for immunogenicity include 1. Post-vaccination seroprotection rates: the proportion of subjects with HAI titers (? 1:40) for influenza strains following each vaccination. 2. Post-vaccination geometric mean of anti-HAI titers for influenza strains following each vaccination. 3. Post-vaccination GMTs of anti-pertussis (PT, FHA, PRN, and FIM), tetanus, diphtheria, and pneumococcal antigens..</p> <p>Data analysis plan: The number of subjects enrolled and their age at enrollment (mean, median, and minimum and maximum), sex, and ethnic origin will be summarized for each group, as well as the number and description of protocol violations.</p> <p>Continuous variables will be presented by summary statistics (eg, mean and standard deviation</p>		

for the non-immunogenicity endpoints, and geometric means and their confidence intervals for the immunogenicity endpoints), and categorical variables will be presented by frequency distributions (frequency counts, percentages, and their confidence intervals).

**Progress:** This protocol was reported completed in July 2007. A total of fifteen subjects enrolled in the study at MAMC; two subjects in Group 1 and thirteen subjects Group 2. Twelve subjects completed all study interventions, and three withdrew prior to completing the study interventions: one moved from the area, one was withdrawn at the parent's request, and one was withdrawn by the PI due to non-compliance. The final report for this protocol should be available in January 2008.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205139	<b>Status:</b> Ongoing
<b>Title:</b> The Impact of Human Metapneumovirus Versus other Common Respiratory Viruses in Infants in Fulltime Daycare		
<b>Principal Investigator:</b> COL (Ret) Mary P. Fairchok, MD		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Sue E. Chambers, RN; Melinda L. Behrens, MD; MAJ Loranee E. Braun, MC; Janet Englund, MD		
<b>Start - Completion:</b> 25 Jan 2006 - Oct 2006	<b>Funding:</b> UW via The Geneva Foundation	<b>Periodic Review:</b> 25 Sep 2007

**Study Objective:** To determine the impact of common respiratory viruses on infants attending fulltime daycare. Specific objectives include the comparison of duration, lost days from daycare, complications and incidence of the viruses studied in this population.

**Technical Approach:** We will be performing a prospective descriptive study on the duration, clinical characteristics, lost days from daycare, complications and incidence of the viruses studied, with particular attention to the comparison of these characteristics of HMPV infection relative to the other viruses studied. We will conduct rolling enrollment up to 125 subjects/month attending at least 20 hours of daycare per week at one of the Fort Lewis Daycare Centers. Subjects enrolled will be 6 weeks-24 months on enrollment. We will obtain baseline enrollment clinical and demographic data and we will then follow-up with all subjects via mailers or telephone calls on a monthly basis, as well as with notices posted at the daycare, to determine presence of development of acute upper respiratory tract infections. If any 2 out of our 5 defined symptoms for respiratory tract infection should develop, subjects will be given a study visit. At that visit, a standardized health questionnaire will be completed, and a nasal swab for reverse transcriptase pcr for Respiratory Syncytial Virus, Human Metapneumovirus, Parainfluenza 1,2,3 and 4, rhinovirus, coronavirus, influenza A and B viruses, and adenovirus will be obtained. A separate clinical visit with a health care provider will be provided if additional assessment and intervention is necessary. Any positive pcrs would then undergo quantitative assay. Parents will be provided with a diary to complete and mail back recording symptoms and duration of the illness as well as impact on work and daycare. Parents will be called for any positive pcr results and given further information about the virus identified. All subjects will be followed from the time of enrollment until 31 October 2006 unless disenrolled. Outcome variables include the incidence of acute upper respiratory tract infections attributable to HPMV versus the other study viruses in the population, attack rate of each virus in the daycare per month, characteristics of the viral infections, impact on the family in days missed from work or daycare, and duration of infection. Co-infection with other respiratory pathogens and secondary infections will also be recorded. Method of analysis of these variables will be conducted using descriptive statistics

**Progress:** A total of 97 subjects have enrolled in this study since January 2006. Since enrollment 48 subjects withdrew: 17 for ineligibility (child removed from daycare or at daycare less than 20 hours per week) and 31 moved from the Fort Lewis area. The remaining 49 subjects are receiving ongoing study treatment per protocol. Subject enrollment continues.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207119	<b>Status:</b> Ongoing
<b>Title:</b> Utilizing Cerebral Spinal Fluid Polymerase Chain Reaction (CSF PCR) to Reveal Unsuspected Varicella-Zoster Meningitis		
<b>Principal Investigator:</b> COL (Ret) Mary P. Fairchok, MD		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Jeffrey R Limjuco, MC; LTC Helen B. Viscount, MC		
<b>Start - Completion:</b> 24 Aug 2007 - 09/07	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this protocol is to determine the proportion aseptic meningitis cases caused by Varicella-Zoster Virus (VZV) isolated in the MAMC Clinical Microbiology Lab. Secondly, to compare the clinical course of aseptic meningitis caused by VZV through chart review

**Technical Approach:** Investigators will be performing a retrospective descriptive study on the proportion of CSF samples containing VZV and the clinical significance of VZV in the setting of aseptic meningitis. CSF samples, which have already been tested via PCR by the lab in cases of aseptic meningitis for VZV, will be reviewed as well as HSV I, HSV II, and Enterovirus. In addition, chart reviews will be performed to document the clinical course of aseptic meningitis with VZV versus HSV I, HSV II, and Enterovirus in patients with aseptic meningitis. Factors to be described include: presenting symptoms, presence of rash on physical exam, treatment regimen, and other CSF study results to include WBC count in CSF, % PMNs in CSF, RBC count in CSF, protein in CSF, and glucose in CSF.

**Progress:** This minimal risk protocol received final approval by the Expedited Review Committee, effective 24 August 2007.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206035	<b>Status:</b> Completed
<b>Title:</b> Military Children at Risk - Enhancing Quality of Life (mCARE) Needs Assessment		
<b>Principal Investigator:</b> Karen L. Fitzgerald, RN, PhD		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Janice L. Hansen, PhD; Virginia F. Randall; Jason P. Cervenka		
<b>Start - Completion:</b> 20 Dec 2005 - Dec 2006	<b>Funding:</b> TATRC via	<b>Periodic Review:</b> 12 Feb 2007

**Study Objective:** The objectives of this study are to (1) delineate the needs of children with life-threatening illnesses and their families who are eligible for care in the Military Health System (MHS), (2) delineate the educational needs of pediatricians (pediatric residents, general pediatricians and pediatric sub-specialists) that relate to providing and coordinating care for children with life threatening illnesses and their families, (3) analyze the TRICARE benefit and services provided by the MHS in relation to the needs of children with life threatening illnesses and their families, and (4) develop recommendations for a program to provide health care services to military children with life threatening illnesses and their families.

**Technical Approach:** This proposal describes Phase II of a needs assessment of military families with children with life-threatening illnesses, using a case study methodology. Phase I of the study (previously funded) includes case studies for the National Capital Area (NCA) and Keesler AFB. Phase II will include case studies of the areas surrounding the Madigan Army Medical Center, Naval Medical Center, San Diego Munson Army Health Clinic at Ft. Leavenworth, Kansas. Altogether, there will be case studies of the NCA, areas surrounding installations with major medical centers for the Army, Navy and Air Force, and the area surrounding a small installation with limited services available through the direct-care military health system. At each site, data collection will include interviews and/or focus groups with parents, interviews and focus groups with health care providers, and collection of TRICARE data regarding case management and utilization of care. Three existing surveys (the FACCT End-of-Life Survey, Medical Home Assessment Tools, and a survey of the quality of life of caregivers previously developed by the investigators with parent advisors), consultation with the mCARE project team and consultation with parent advisors will provide the basis for interview and focus group questions. Needs identified will be compared to the services available at each site and then to the services covered by the TRICARE benefit (as analyzed in Phase I of the needs assessment). In collaboration with other partners in the mCARE project, needs identified by parents of children with life-threatening illnesses and health care providers who provide care for them will be compared to services provided by the military health care system, the TRICARE benefit, and community resources. The assessment will also describe access and barriers to access for services from these three sources. Subsequently, the mCARE project team will propose a model of care for military children and their families that will provide a coordinated, comprehensive, family-centered approach to care from the time of diagnosis of a life-threatening illness through the time of bereavement of families. This proposal also adds the following components to the needs assessment as described in the Phase I proposal: development of an advisory group of parents in the National Capitol Area, a collaboration with Family Medicine, adaptation to this population of a previously-developed measure of quality of life of caregivers, technical assistance in defining eligibility criteria, and participation in evaluation of program components piloted by other mCARE project team members (respite care and/or care coordination).

**Progress:** This protocol was completed during FY07, with 28 healthcare providers and 35 parents enrolled for an overall total of 63 subjects who completed the study since May 2006. Fifteen (15) final themes were delineated to include: Theme Group One: Systems (1) Access to Health Care

and Services, (2) Care Coordination, (3) Long-term Care Needs, (4) Medical Home, (5) Military Health System Roles and Administration. Theme Group Two: Relationships (6) Advocacy, (7) Relationships and Communication with Healthcare Providers 8. Decision Making. Theme Group Three: Family Needs (9) Social and Emotional Needs, (10) Financial Toll, (11) Search for Meaning/Spiritual Care. Theme Group Four: Palliative Care (12) Palliative Care, (13) End-of-Life Care. Theme Group Five: Education, (14) Education for Healthcare Providers and Families. Theme Group Six: Military, (15) Military Issues.

Results of the MHS analysis indicate that children with LTC who are entitled to services from the MHS do not receive care in the comprehensive pediatric palliative care and hospice model called for by the Institute of Medicine, Medicaid, the Children's Hospice International, and the National Quality Forum. An estimated 4000 children with LTC are eligible for medical care through the MHS each year. Approximately 400 of these children die each year. An independent government cost estimate of a comprehensive palliative and hospice program for children, however, demonstrates that a net cost savings would be obtained by the MHS within a few years of implementing such a program. Some key features of a pediatric palliative care and hospice program are not available to most children with LTC in the MHS. For example, CHAMPUS/TRICARE authorizes extended home health care only to children who meet a high threshold of disability and who are dependents of active duty service members. Hospice is authorized as a benefit only when it meets Medicaid criteria (begins within six months of expected death, and patient must forgo disease-directed care). Bereavement counseling is explicitly excluded as a benefit under CHAMPUS/TRICARE unless the beneficiary meets a definition of mental illness.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207003	<b>Status:</b> Ongoing
<b>Title:</b> Effects of Deployment in Military Children on General Health, School Performance and Health Care Utilization		
<b>Principal Investigator:</b> Capt Eric M. Flake, MC, USAF		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Beth E. Davis, MC; Patti L. Johnson, Ph.D.		
<b>Start - Completion:</b> 17 Oct 2006 - Sep 2008	<b>Funding:</b> The Geneva Foundation	<b>Periodic Review:</b> 10 Oct 2007

**Study Objective:** The objective of this study is to evaluate school age children during deployment by measuring general psycho-social health, school performance and health care utilization by interviewing their parents and providing them with a questionnaire to fill out.

**Technical Approach:** Early Deployment (deployment month 1-6). Step 1: Identify which families have children attending elementary school that has a deployed parent. These participants will be identified from the Family Readiness Groups and self referral. Step 2: Mail and E-mail a flyer requesting the family's participation in the study. Step 3: When a patient responds showing willingness to participate will proceed to send them a starter packet which includes, a study description, informed consent form, demographic questionnaire, the Parenting Stress Index-Short Form, the Pediatric Symptom Checklist and a SASE to return the questionnaires. When signing the consent for participation that parent will also be asked to sign a school release of information form which would allow acces to the child's academic report care for 2006-2007.

Late Deployment (deployment month 6-12+). Step 5: The same families initially enrolled will be mailed out the Parenting Stress Index - Short Form, the Pediatric Symptom Checklist and a SASE.

July 2007 - January 2008. Step 6: All data is gathered and organized. Obtaining School data: Request will be made to the schools to provide academic report card for 2006-2007 school year. Obtaining Health care utilization data: Data from the servicemember months of deployment will be evaluated and significant findings if any will be reported. This will be done by a electronic and paper record review of all health related encounters.

**Progress:** This minimal risk protocol received approval by the Expedited Review Committee 17 October 2006. A total of 116 spouses of deployed service members were enrolled in this study during FY 07; 15 of the surveys were not entirely complete. Data Analysis is underway for the 101 complete surveys using Excel and SPSS to determine statistically significant trends and comparisons. Preliminary data is being prepared to be submitted to USPS. Over the past year in addition to recruiting volunteers for this study, efforts have been made to support deployed spouses by attending and speaking at FRG meetings, pre and post deployment briefings and participating in community deployment support fairs. Enrollment remains ongoing.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 97054	<b>Status:</b> Ongoing
<b>Title:</b> POG 9426: Response Dependent Treatment of Stages IA, IIA, and IIIA(1-micro) Hodgkin's Disease with DBVE and Low Dose Involved Field Irradiation with or without Zinecard		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 21 Mar 1997 - Indef	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 15 Feb 2005

**Study Objective:** (1) To tailor chemotherapy courses based on the patients' initial response to therapy, (2) To examine the activity of variable courses of doxorubicin, bleomycin, vincristine, and etoposide (DBVE) and low-dose involved field irradiation, (3) To monitor safety and feasibility of the response-dependent approach, and morbidity, immediate and long term toxicities of the above regimen, (4) To evaluate if limited therapy is adequate for patients with early response, (5) To examine if addition of Zinecard can reduce pulmonary toxicity while not significantly reducing response rate or event-free survival, and (6) To determine if the frequency and magnitude of myocardial injury during therapy, as measured by an elevation of cardiac Troponin-T in the serum, is reduced by the addition of Zinecard.

**Technical Approach:** Registered study patients will be randomized to receive the investigational drug Zinecard just prior to the administration of the chemotherapy drugs bleomycin and doxorubicin. Following disease staging with radiologic imaging and laboratory evaluations, patients will receive 2 courses of the four drug combination etoposide, vincristine, bleomycin and doxorubicin at 28 day intervals. Patients will be restaged after receiving these two chemotherapy courses. Those showing remission will go on to radiation therapy, while those showing residual disease will receive 2 more courses of the four drug combination and then go on to radiation therapy. Follow-up will continue for a minimum of 10 years at least on a yearly basis.

**Progress:** This protocol was reactivated in July 2007, to continue follow-up of two subjects enrolled. The protocol had been terminated in August 2005, to allow long term follow-up to be conducted under COG-LTF Protocol, #205105; however, study staff decided to discontinue use of the LTF protocol.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 98065	<b>Status:</b> Ongoing
<b>Title:</b> POG P9641: Primary Surgical Therapy for Biologically Defined Low-Risk Neuroblastoma; A COG Phase III Intergroup Study		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 3 Aug 2007 - Indef	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 17 Feb 2005

**Study Objective:** (1) To determine if low risk INSS stage 2A/2B asymptomatic neuroblastoma patients treated with surgery alone will have a three year survival (S) rate of 95%, (2) To determine if low risk INSS stage 1 asymptomatic neuroblastoma patients treated with surgery alone will have a three year S rate of 95%, (3) To determine if low risk INSS stage 4S asymptomatic neuroblastoma patients treated with surgery alone will have a three year S rate of 95%, (4) To estimate the response and 3 year event-free survival (EFS) rates of symptomatic patients with chemotherapy, (5) To estimate the EFS and S rates in patients who relapse or progress after initial treatment with surgery alone, (6) To determine the acute and long-term morbidity/toxicities associated with treating low-risk neuroblastoma with surgery alone or with surgery and chemotherapy, (7) To further define and evaluate the prognostic importance of other biologic factors as determined on studies POG #9047 (or its successor), CCG #B973, and by International Neuroblastoma Risk Group criteria, (8) To collect resource utilization data regarding number of hospital days, the extent of transfusion support, and the use of diagnostic imaging, and to compare these with historical CCG study 3881 data.

**Technical Approach:** Patients in this study will be stratified by stage and extent of disease to either surgery alone or surgery with chemotherapy. Further studies done on patient's tumor specimens may change their classification to "intermediate" or "high" risk neuroblastoma, in which case they will be taken off study and more intensive chemotherapy will be administered.

**Progress:** This protocol was reactivated in July 2007, to continue follow-up of one subject enrolled. The protocol had been terminated in August 2005, to allow long term follow-up to be conducted under COG-LTF Protocol, #205105; however, study staff decided to discontinue use of the LTF protocol.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 98090	<b>Status:</b> Ongoing
<b>Title:</b> COG P9442: National Wilms Tumor Late Effects Study		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieuw, MC		
<b>Start - Completion:</b> 17 Jul 1998 - Indef	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 12 Jun 2007

**Study Objective:** To determine (1) the frequency of Wilms tumor and other cancers in family members of Wilms tumor patients in order to estimate the recurrence risk in siblings and offspring; test the plausibility of specific genetic modes of inheritance in homogeneous subgroups; and identify familial cancer syndromes (if any) that may involve Wilms tumor, (2) To determine fertility rates of Wilms tumor patients and rates of perinatal mortality, low birth-weight and adverse pregnancy outcomes in relation to the type and amount of cancer treatment received in childhood, (3) To estimate the rates of selected congenital defects and of specified single gene disorders (sentinel phenotypes) in the offspring of Wilms tumor patients, (4) to estimate the rates of second malignancy neoplasms in relation to the dosage of radiation therapy and the use of specific chemotherapeutic agents (Actinomycin D, doxorubicin, Cytosine and etoposide) received in childhood, (5) to compare the incidence rate of congestive heart failure among Wilms tumor survivors in relation to the dose of radiation therapy received to abdomen and/or lungs and to the use of specific chemotherapeutic agents.

**Technical Approach:** The large number of Wilms tumor survivors ascertained by the NWTS during its first twenty years of operation constitutes an ideal cohort for the study of familial risk and late effects of treatment. Four protocol studies have been conducted; treatment protocols and results for the first three studies have been published. A large fraction of the total national U.S. incidence of Wilms tumor has been registered on these studies, probably as much as 70% of an estimated 450-500 cases occurring nationally since 1980. Over 2,500 children who were followed on NWTS treatment protocols have now survived 5 or more years since their original diagnosis. Many of those treated more than a decade ago have reached sexual maturity, so that their reproductive history and the status of their offspring may be evaluated by entry into this study.

**Progress:** This minimal risk protocol remains open to enrollment, with two subjects enrolled; one subject transferred to another institution and one continued to be followed at MAMC during FY07. A change in the role of PI from Dr. Lieuw to Dr. Forouhar was submitted and approved.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 200048	<b>Status:</b> Ongoing
<b>Title:</b> POG P9851: Osteosarcoma Biology Protocol, Companion to Group-Wide Therapeutic Studies		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieuw, MC		
<b>Start - Completion:</b> 22 Feb 2000 - Feb 2010	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 22 Jan 2008

**Study Objective:** (1) To increase our understanding of the basic biology of these tumors, with a distinct possibility that new therapeutic targets may be uncovered. Examples of this type are ErbB-2 and methotrexate resistance factors, (2) To develop a set of biologic prognostic indicators which can be measured at diagnosis and which will be predictive of response and outcome in osteosarcoma. These could then be used in subsequent treatment programs to determine therapy, avoiding excessive toxicity to good risk patients and reserving alternative, more intensive therapy for those at standard risk. Examples include loss of heterozygosity at Rb and MDR, (3) To determine the feasibility of various assays and to develop a reliable mechanism of distributing osteosarcoma samples to various intergroup investigators, with centralized reporting of laboratory results and adequate quality control.

**Technical Approach:** At the time of biopsy or surgery (definitive or recurrence), tumor tissue that is not needed for diagnosis will be processed and forwarded to the Cooperative Human Tissue Network (CHTN) for distribution. Specimens will include: tumor tissue (Formalin-fixed or formalin-fixed paraffin embedded block or 30 unstained slides; blood samples (heparinized (10 ml), serum (14 ml)). Assays being performed: MDR Immunohistochemistry (University of Rochester); MDR Functional Assays/MRP (Memorial Sloan-Kettering); Methotrexate Transport & Metab (Memorial Sloan-Kettering); Topoisomerase II (Yale University); Bcl-2/Bax (Yale University); Rb/p53 (Fels Institute); ErbB-2 (Memorial Sloan-Kettering); MDM2 (Memorial Sloan-Kettering); p16/p21 (Hospital for Sick Children); LOH at 3q,18q (Fels Institute); sis,gli,fos (Yale University); SV40 (University of Colorado); myc,RAS (Memorial Sloan-Kettering); metalloproteinase (Yale University); c-met/HGF (Yale University); IGF-I/IGF-IR (University of Maryland); Telomerase (St. Jude Children's); Ploidy (Dana Farber).

**Progress:** In July 2006, COG reported that this companion protocol would be phased out and expected to close accrual within six months after the new protocol was up and running. One subject enrolled at MAMC in 2002, and continued to be followed during FY07 pending close-out of this protocol by COG. A change in the role of PI from Dr. Lieuw to Dr. Forouhar was submitted and approved.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 200049	<b>Status:</b> Ongoing
<b>Title:</b> COG D9902, A COG Soft Tissue Sarcoma Diagnosis, Biology and Banking Protocol		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieuw, MC		
<b>Start - Completion:</b> 22 Feb 2000 - Feb 2010	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 22 Jan 2008

**Study Objective:** (1) To facilitate the collection of human tissue and other biologic specimens (blood, bone marrow) from Intergroup Rhabdomyosarcoma Study Group (IRSG) investigators, (2) To provide a repository for long-term storage of tissue and other biologic specimens (blood, bone marrow) collected by IRSG investigators (referred to as the Bank), and (3) To make available, through the IRSG/Cooperative Human Tissue Network, these materials for approved projects by laboratory-based investigators.

**Technical Approach:** At the time of initial diagnosis of rhabdomyosarcoma or undifferentiated sarcoma (or at re-excision of the primary tumor, if it occurs prior to the start of chemotherapy), surgical tissue, bone marrow and blood that are no longer needed for diagnosis will be prepared and shipped to the Pediatric Cooperative Human Tissue Network (CHTN) for Banking and Distribution.

**Progress:** This protocol remains open to enrollment with two subjects enrolled, both have moved out of the MAMC area. Follow up data is not required under this tissue banking protocol. Amendment #8 and #9 changes to the protocol were submitted and approved, along with a change in the role of PI from Dr. Lieuw to Dr. Forouhar during FY07.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 200076	<b>Status:</b> Ongoing
<b>Title:</b> COG 9905, ALinC 17: Protocol for Patients with Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL), A Phase III Study		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 3 Aug 2007 - Indef	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 6 May 2005

**Study Objective:** (1) To determine in a randomized trial, if a delayed multi-drug intensification, administered in the context of intensive anti-metabolite therapy, will improve outcome for children with ALL. This objective will also be assessed as part of POG protocol 9904; (2) In conjunction with POG 9904, to compare short MTX infusion (2g/m<sup>2</sup> over 4 hours) with a longer infusion (1g/m<sup>2</sup> over 24 hours), primarily with respect to efficacy and secondarily with respect to toxicity; (3) To determine the correlation between event-free survival (EFS) and the following measures of minimal residual disease (MRD)/early response (ER): (a) the rate of peripheral blast count disappearance and the absolute blast count on day 8 as determined morphologically, by flow cytometry and using molecular techniques; (b) Marrow morphology on day 8, and; (c) MRD as determined by flow cytometry and molecular techniques on bone marrow and peripheral blood samples on day 29 and after consolidation; (4) Using a case control design, quantitate MRD with flow cytometry and molecular techniques, to determine whether late relapse correlates with a given level of MRD in marrow samples obtained and banked at the completion of therapy. To analyze samples obtained at relapse to ascertain whether markers of MRD remain constant i.e., if a relapse not "predicted" by high levels of MRD in remission samples, is it because of a change in the identified markers; (5) To determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction); (6) To determine the relationship between a membrane bound glucocorticoid receptor and EFS via quantitation of the glucocorticoid receptor concentrations in marrow samples at diagnosis.

**Technical Approach:** This study will utilize a 2 x 2 factorial design to answer two randomized questions. The standard arm will recapitulate regimen A of the current POG protocol for standard risk patients. Induction will include three or four drugs (dependent on initial risk classification POG 9900) and consolidation will include 24-hour MTX infusions, at one gram per square meter, given every three weeks for a total of six doses. The two randomizations will assign patients to receive therapy with or without the delayed intensification and receive the IV MTX as a 2 gm/m<sup>2</sup> infusion over four hours versus a one gram per m<sup>2</sup> infusion over 24 hours. Intensive continuation will include 4 cycles of therapy with each 12 week cycle including 6 courses of divided dose oral MTX, nightly 6-MP, a dose of intrathecal MTX and a pulse of vincristine and dexamethasone. Standard continuation therapy includes weekly MTX, daily 6-MP and vincristine/dexamethasone pulses every 16 weeks. Dexamethasone replaced prednisone in the 9705 pilot study, and will be utilized here because of better CNS penetration and data suggesting that its use enhance event-free survival. The current POG study for standard risk patients includes a randomization to single versus twice daily dosing of oral 6-MP, based on the concept that duration of exposure is critical to anti-metabolite efficacy. This study includes only the traditional single nightly dose. Should the results of the open trial suggest an advantage to the use of divided dose 6-MP, this protocol will be amended.

**Progress:** This protocol was reactivated in July 2007, to continue follow-up of seven subjects enrolled. The protocol had been terminated in August 2005, to allow long term follow-up to be

conducted under COG-LTF Protocol, #205105; however, study staff decided to discontinue use of the LTF protocol.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 200077	<b>Status:</b> Ongoing
<b>Title:</b> COG 9904, ALinC 17: Treatment for Patients with Low Risk Acute Lymphoblastic Leukemia, A Phase III Study		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Kenneth H. Lieuw, MC; COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 12 May 2000 - May 2004	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 24 Apr 2007

**Study Objective:** (1) In conjunction with POG 9905, to compare short MTX infusion (2g/m<sup>2</sup> over 4 hours) with a longer infusion (1g/m<sup>2</sup> over 24 hours), primarily with respect to efficacy and secondarily with respect to toxicity. (2) to determine in a randomized trial, if a delayed multi-drug intensification, administered in the context of intensive anti-metabolite therapy, will improve outcome for children with ALL, (3) To determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction), and (4) To determine the relationship between a membrane bound glucocorticoid receptor and EFS via quantitation of the glucocorticoid receptor concentrations in marrow samples at diagnosis.

**Technical Approach:** This protocol will randomize between the 4-hour and 24 hour methotrexate infusion and for patients with TEL/AML1 gene, between standard and delayed intensification. Data from POG 9904 and 9905 will be pooled for statistical analysis of efficacy and toxicity. This study will determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction). Induction will include three or four drugs (dependent on initial risk classification POG 9900).

**Progress:** This protocol closed enrollment in April 2005, with four subjects enrolled, who have completed study treatment and continued to be followed at MAMC during FY07. No adverse events were reported. A change in the role of PI from Dr. Lieuw to Dr. Forouhar was submitted and approved during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 200139	<b>Status:</b> Ongoing
<b>Title:</b> COG A5971: Randomized Phase III Study for the Treatment of Newly Diagnosed Disseminated Lymphoblastic Lymphoma or Localized Lymphoblastic Lymphoma, A Phase III COG Study		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieu, MC		
<b>Start - Completion:</b> 26 Sep 2000 - Sep 2007	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 21 Aug 2007

**Study Objective:** (1) To compare the event free survival and survival in patients with disseminated lymphoblastic lymphoma treated on four regimens. (NHL/BFM-95 vs. CCG BFM), (2) To determine if treatment with a regimen without high dose methotrexate will maintain the same excellent disease free survival obtained with NHL/BFM-90, (3) To determine if intensification with anthracycline and cyclophosphamide improves disease free survival, (4) To collect outcome data on uniformly treated patients with localized disease or CNS positive disease, and (5) To determine if rapid reduction in tumor volume as defined by chest radiography and CT is predictive of improved outcome.

**Technical Approach:** Patients with disseminated (Murphy stage III or IV) lymphoblastic lymphoma without evidence of CNS disease will be randomized to one of four treatment regimens: Standard CCG BFM (regimen A1); CCG BFM intensified with cyclophosphamide/anthracycline intensification during the induction and delayed intensification phases (regimen A2); Standard NHL/BFM-95 (regimen B1); or NHL/BFM-95 intensified with cyclophosphamide/anthracycline intensification during the induction and delayed intensification phases (regimen B2). Patients with disseminated lymphoblastic lymphoma positive for CNS disease will be assigned to the intensified NHL/BFM-95 arm (regimen B2) with delayed radiation therapy. Patients with localized lymphoblastic lymphoma (Murphy stage I or II) will be assigned to the standard CCG BFM arm without additional intrathecal methotrexate (regimen A0). The duration of each treatment arm is 2 years and consists of Induction, Consolidation, Interim Maintenance, Delayed Intensification, and Maintenance therapies.

**Progress:** This protocol closed enrollment in July 2007, with one subject enrolled in 2004, who is currently being treated at WRAMC. Responsibility for data submission to COG for this patient has not been officially transferred to WRAMC; therefore the protocol remains ongoing at MAMC. A change in the role of PI from Dr. Lieu to Dr. Forouhar was submitted and approved during FY07.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 201108	<b>Status:</b> Ongoing
<b>Title:</b> COG ANBL00B1, Neuroblastoma Biology Studies		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieuw, MC		
<b>Start - Completion:</b> 26 Jun 2001 - May 2007	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 22 May 2007

**Study Objective:** (1) To prospectively analyze the factors that are currently used for risk-group assignment (DNA content by flow cytometry, MYCN copy number by FISH, and tumor histology using the International Neuroblastoma Pathologic Classification System) in neuroblastoma tumors at the time of diagnosis, (2) to maintain a reference bank containing clinically and genetically characterized frozen tumor tissue, tumor DNA and RNA, tumor touch preparations, histology slides and blocks, cell lines, and paired normal DNA obtained at the time of diagnosis (all patients), at the time of second-look surgery (high-risk patients), and relapse (all patients) for future research studies, (3) to prospectively analyze the prevalence of 1p, 11q, 14q LOH and gain of 17q; the expression of nerve growth factor (NGF) and its high affinity (Trk-A) and low affinity (p75 NTR) receptors; and telomerase activity in diagnostic neuroblastoma tumors, and to determine the independent clinical significance of these biologic factors compared to MYCN amplification, INSS stage, age, and histologic variables in predicting either response to treatment or outcome, (4) to build a database of the known biologic prognostic factors for patients on therapeutic studies, (5) to serve as a Registry for neuroblastoma patients whose tumors demonstrate clinical and genetic features defined as "Low Risk" for treatment failure in the absence of adjuvant therapy, and (6) A secondary objective of this study is to prospectively analyze the role of ferritin, LDH, and Imaging-defined risk factors identified at the time of diagnosis in risk assessment.

**Technical Approach:** Clinical and biological factors have been shown to have prognostic value in neuroblastoma. Current therapeutic studies for neuroblastoma patients are tailored according to patient risk. In the Children's Oncology Group (COG), risk-group assignment is currently based on INSS stage, age, MYCN copy number, tumor cell ploidy, and Shimada tumor histopathology. However, additional factors have also been shown to have prognostic value including the level of Trk-A expression, multi-drug resistance associated protein (MRP) expression, telomerase activity, CD44 expression, and genetic abnormalities including LOH of 1p, 11q, 14q and gain of 17q. We hypothesize that analyzing additional genetic and biologic factors will result in a further refinement of the current COG risk-group schema, and will, thereby, impact future risk-based approaches to therapy. We further hypothesize that maintaining tumor and nucleic acid banks with well characterized samples will provide invaluable biologic resources for future research studies that will lead to a further understanding of neuroblastoma biology and the development of new, effective therapy for high-risk patients.

**Progress:** This protocol remains open to enrollment with three subjects enrolled at MAMC, one during FY07. One subject transferred to Seattle Children's Hospital in July 2006. Data collection continues on the two remaining subjects. Amendment #7 and a change in the role of PI from Dr. Lieuw to Dr. Forouhar were submitted and approved at the time of this report.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203024	<b>Status:</b> Ongoing
<b>Title:</b> COG AHOD0031, A Phase III Group-wide Study of Dose-intensive Response-based Chemotherapy and Radiation Therapy for Children and Adolescents with Newly Diagnosed Intermediate Risk Hodgkin Disease		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieu, MC		
<b>Start - Completion:</b> 13 Jan 2003 - Mar 2008	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 11 Dec 2007

**Study Objective:** (1) To compare response-based therapy to standard therapy for intermediate risk Hodgkin disease. (2) To determine whether involved field radiation therapy (IFRT) can be eliminated based upon early and complete response to multiagent chemotherapy. (3) To determine whether the addition of an additional two cycles of chemotherapy (DECA) can improve outcome in those with a slow early response to standard chemotherapy. (4) To prospectively collect information on the individual prognostic significance of the following presenting factors: erythrocyte sedimentation rate, circulating levels of IL-100, each of the "B" symptoms - fever, night sweats, weight loss, nodal aggregate > 6cm, large mediastinal mass > 1/3 thoracic diameter and number of involved nodal sites, histology, albumin, blood counts, sex and age. (5) To study the reliability and utility of [18F] - Fluorodeoxyglucose (FDG) Imaging (PET scans) as an imaging modality in Hodgkin disease. (6) To determine the frequency and severity of late effects of therapy including thyroid dysfunction, infertility, cardiotoxicity, pulmonary toxicity and second malignant neoplasms. (7) To serve as the therapeutic companion to biology and late effects studies in Hodgkin disease and correlate those results with response to therapy, event free-survival and overall survival.

**Technical Approach:** All patients will receive 3 cycles of ABVE-PC three weeks apart followed by a re-evaluation of disease. Those with a rapid early response will receive an additional 1 cycle of ABVE-PC three weeks later followed by another re-evaluation of disease. Rapid early responders, who have sustained a complete response following a total of 4 cycles of ABVE-PC chemotherapy, will be randomized to omit (reduced therapy arm) or receive consolidative low dose involved field radiation therapy (IFRT) (standard therapy arm). Those with less than a complete response will receive IFRT. Patients with a slow early response to 3 cycles of ABVE-PC will be randomized to receive 1 additional cycle of ABVE-PC (standard therapy arm) alone versus 1 additional cycle of ABVE-PC preceded by 2 cycles of DECA (augmented therapy arm). All patients who are slow early responders will receive consolidative low dose IFRT. Patients with less than a complete response after consolidative radiation therapy or those with progressive disease at any time will be treated at the discretion of the treating physician after consultation with the study chair.

**Progress:** This protocol remains open to enrollment with a total of four subjects enrolled thus far, one during FY07. All subjects have completed study treatment and continue to be followed. Amendment #3 and a change in the role of PI from Dr. Lieu to Dr. Forouhar were submitted and approved. No adverse events were reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205014	<b>Status:</b> Ongoing
<b>Title:</b> COG AHOD0321, A Phase II Study of Weekly Gemcitabine and Vinorelbine in Children with Recurrent or Refractory Hodgkin Disease		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieuw, MC		
<b>Start - Completion:</b> 6 Dec 2004 - Dec 2005	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 23 Oct 2007

**Study Objective:** To determine the response rate after weekly administration of the combination of gemcitabine and vinorelbine to patients with recurrent or refractory Hodgkin Disease. To document the toxicity of weekly administration of gemcitabine and vinorelbine in patients with recurrent or refractory Hodgkin Disease.

**Technical Approach:** This is a Phase II study of weekly Gemcitabine and Vinorelbine In children with recurrent or refractory Hodgkin Disease. This study will evaluate the use of a new re-induction chemotherapy regimen consisting of the anti-cancer drugs combination of gemcitabine and vinorelbine in patients who have previously been treated for Hodgkin Disease. Patients will receive at least two cycles (21 days each) of weekly GEM/VINO therapy. The goal is to determine if the combination of these is active against recurrent Hodgkin Disease and to find out what effects this drug combination will have. Patients with any response after the first two cycles may elect to proceed directly to stem cell transplantation. Those with stable disease after the first two cycles, will receive a minimum of two more cycles of GEM/VINO. At the end of the fourth cycle, patients without progressive disease can remain on study and continue to receive GEM/VINO or go off study for alternative therapy. About 26 patients between the ages of 0 to <30 years of age will be participating in this study.

**Progress:** This protocol closed to enrollment in June 2007, with one patient enrolled and continuing to be followed after having had a transplant procedure. A change in the role of PI from Dr. Lieuw to Dr. Forouhar was approved during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205015	<b>Status:</b> Ongoing
<b>Title:</b> COG AALL0031, A COG Pilot Study for the Treatment of Very High Risk Acute Lymphoblastic Leukemia in Children and Adolescents		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Kenneth H. Lieuw, MC; COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 5 Apr 2005 - Jun 2005	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 23 Oct 2007

**Study Objective:** Primary Objective: To determine the feasibility in terms of patient accrual and toxicity of an intensified chemotherapeutic regimen incorporating novel agents for treatment of children and adolescents with very high risk (VHR) ALL. Secondary Objectives: (1) To determine if the BCR-ABL-specific tyrosine kinase inhibitor STI571 can be incorporated into this regimen with acceptable toxicity for patients with Ph+ ALL. (2) To compare EFS for VHR patients treated with the intensive chemotherapy with that of historical controls. (3) To conduct a preliminary evaluation of the feasibility and efficacy of following intensive consolidation by Hematopoietic Stem Cell Transplantation (HSCT) as therapy for patients with HLA matched related donors. (4) To determine if MRD assessed at the end of induction and prior to reinduction and prior to HSCT therapy by PCR and flow cytometry can predict relapse. (5) To evaluate whether MRD detected by PCR at post-intensification time points is prognostically significant. (6) To evaluate whether gene expression patterns can be identified by microarray evaluations to predict disease recurrence or response to STI571.

**Technical Approach:** This pilot study will utilize a novel intensified chemotherapeutic regimen for VHR patients based on (1) the use of ifosfamide and etoposide in POG ALL relapse studies; (2) the use of high dose methotrexate for children and infants; and (3) the intensive CCG New York II regimen used for patients with lymphomatous ALL. The study will determine whether an adequate number of VHR patients will be accrued to form the basis for development of a future phase III trial within the COG. The presence or absence of minimal residual disease in patients in remission also will be determined. If the intensive treatment is found to have acceptable toxicity and shows potential, either alone, or with transplant, for improving outcome of the VHR patient population, it will be the first promising strategy identified for this group. The accrual goal is 110 patients over a 2 year time frame.

**Progress:** This protocol closed to enrollment in October 2006, with one patient enrolled and continuing to be followed. Multiple external adverse events have been reported. A change in the role of PI from Dr. Lieuw to Dr. Forouhar was approved during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205067	<b>Status:</b> Ongoing
<b>Title:</b> COG AALL03B1, Classification of Acute Lymphoblastic Leukemia		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieuw, MC		
<b>Start - Completion:</b> 11 Jul 2005 - Mar 2015	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 24 Apr 2007

**Study Objective:** To provide a classification guide that will organize the clinical and laboratory data necessary for assigning each patient with newly diagnosed ALL to a specific therapeutic trial. (2) To provide an administrative base to capture classification data for correlative studies accompanying current Children's Oncology Group (COG) ALL treatment protocols. (3) To provide a central reference guide for all required and research only studies that will be conducted at local and reference laboratories for all newly diagnosed patients with ALL. (4) To provide a mechanism for optional banking of leukemia and germ line specimens for current and future research.

**Technical Approach:** This COG risk group classification protocol will serve as a foundation for patients with newly diagnosed ALL. Registration on this protocol will be a requirement for entry onto any COG therapeutic study. The purpose of this classification protocol for ALL is to integrate data from recently completed clinical trials into an organized framework to appropriately risk stratify and treat patients enrolled in COG clinical trials for ALL. Patients will be assigned to an induction treatment regimen on the basis of studies that are performed at the host institution. Additional samples will also be sent by the local institution to one or more COG ALL reference labs at the time of diagnosis and at defined time points during therapy. This data will be used to refine subsequent therapy at the end of induction by assignment to a specific treatment protocol for defined risk groups in non-infant B-precursor ALL and/or via non-randomized allocation to specific treatment regimens within a given trial. The classification study will also be used for participation in companion biology research studies that are not used for treatment allocation and for voluntary banking of leukemia cells for future research. Approximately 8000 people will take part in this study across the United States and abroad. Madigan Army Medical Center plans to enroll 2-3 patients per year.

**Progress:** This protocol remains open to enrollment with three subjects enrolled, one during FY07. All three subjects have been enrolled, and are currently receiving treatment, in COG treatment protocols.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205068	<b>Status:</b> Ongoing
<b>Title:</b> COG AALL0232, High Risk B-precursor Acute Lymphoblastic Leukemia		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieuw, MC		
<b>Start - Completion:</b> 29 Jul 2005 - Mar 2015	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 24 Apr 2007

**Study Objective:** (1) To improve the outcome of children with high risk acute lymphoblastic leukemia. (2) To determine the relative safety and efficacy of dexamethasone given for 14 days versus prednisone given for 28 days during Induction. (3) To determine the relative safety and efficacy of high dose methotrexate (5gm/m<sup>2</sup>) with Leucovorin rescue compared to escalating methotrexate without Leucovorin rescue (Capizzi I) delivered during Interim Maintenance. (4) To correlate Day 29 Minimal Residual Disease (MRD) with Event Free Survival (EFS) and Overall Survival (OS). (5) To correlate early marrow response status with Day 29 MRD status. (6) To improve outcome by identifying additional high risk patients by day 29 MRD for treatment with fully augmented BFM.

**Technical Approach:** This study will compare the use of two steroid drugs, dexamethasone and prednisone, during induction and will examine the best way to give methotrexate during the interim maintenance phase of treatment. This study will use a known chemotherapy regimen that has been very effective for treating children with high risk ALL and test whether two changes to this treatment can cure more patients without increasing side effects. The aim of the first change is to test whether 14 days of dexamethasone is tolerated without an increased number of severe side effects and is better than 28 days of prednisone in decreasing the number of leukemia cells during the first month of treatment. The aim of the second change is to determine whether giving higher doses of methotrexate, during interim maintenance, will work better than giving it on a schedule that starts with a lower dose and increases with each of the later doses.

**Progress:** This protocol remains open to enrollment with two subjects enrolled, none during FY07. One subject failed induction therapy and was taken off study and enrolled on another COG protocol. The other patient continues to receive treatment. No adverse events have been reported.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205084	<b>Status:</b> Ongoing
<b>Title:</b> COG AGCT0132, A Phase III Study of Reduced Therapy in the Treatment of Children with Low and Intermediate Risk Extracranial Germ Cell Tumors		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieuw, MC		
<b>Start - Completion:</b> 25 Nov 2005 - Nov 2009	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 6 Jun 2007

**Study Objective:** Low Risk (LR) (1) To assess whether the proposed therapeutic plan can maintain a 3-year survival of at least 95% for patients newly diagnosed with Stage I gonadal malignant germ cell tumors. (2) To determine the cytogenetic and molecular genetic features which correlate with clinical differences in behavior. These tissues will be banked for future analyses of the biologic characteristics of malignant germ cell tumors.

Intermediate Risk (IR) (1) To assess whether three cycles of 3-day compressed PEB chemotherapy can maintain a 3-year event-free survival of at least 92% for patients with newly diagnosed Stage II-IV malignant testicular and Stage II-III ovarian germ cell tumors, newly diagnosed Stage I-II non-gonadal extracranial malignant germ cell tumors, or relapsed/progressed immature teratomas. (2) To determine the cytogenetic and molecular genetic features which correlate with clinical differences in behavior. These tissues will be banked for future analyses of the biologic characteristics of malignant germ cell tumors. (3) To assess whether three cycles of 3-day compressed PEB chemotherapy can maintain a 3-year survival of at least 95% for patients with newly diagnosed Stage II-IV malignant testicular and Stage II-III ovarian germ cell tumors, newly diagnosed Stage I-II non-gonadal extracranial malignant germ cell tumors, or relapsed/progressed immature teratomas with malignant components.

Cancer Control Objectives (1) To estimate the percentage of patients with Stage I ovarian and Stage I testicular GCTs for whom chemotherapy can be eliminated in the first three years following diagnosis. (2) To estimate the percentage of intermediate risk patients requiring only three cycles of therapy. (3) To delineate the acute toxicities and long term sequelae associated with therapy compression. These will be compared with historical data available from CCG-8882/POG-9049. (4) To determine the number of hospital days and total drug dosages required for the compressed therapy. These will be compared with historical data available from CCG-8882/POG-9049. (5) To compare the number of protocol directed treatment days of CCG-8882 with the number of treatment days used in AGCT0132.

Tumor Biology Objectives (1) To collect samples and facilitate studies of germ cell tumor cytogenetics and molecular genetics including deletion, mutation and imprinting on chromosomes 1 and 6, and amplification of c-myc. (2) To derive tumor cell lines and xenografts of germ cell tumors for use in studies of biologic agents and differentiation agents. (3) To establish a biologic samples bank for germ cell tumors to include frozen tumor and frozen normal tissue that may be used in future studies.

**Technical Approach:** AGCT0132 is a Phase III Study of Reduced Therapy in the Treatment of Children with Low and Intermediate Risk Extracranial Germ Cell Tumors. This study would avoid chemotherapy in low risk testicular/ovarian germ cell tumors by using surgery and observation. If during observation the tumor markers do not return to normal or become abnormal, the patient will be treated with chemotherapy in 3 cycles over a period of 9 weeks. Each treatment will involve 3 anti-cancer drugs: cisplatin, etoposide, and bleomycin. In patients with intermediate risk the standard therapy would be surgery plus chemotherapy. The purpose of this study would be to

decrease the total amount of chemotherapy given from 4 cycles to 3. The number of days chemotherapy would be given would also decrease from 5 to 3 days in each treatment cycle.

**Progress:** This greater than minimal risk protocol received initial IRB approval in November 2005, and remains open to enrollment with no MAMC subjects enrolled to date.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205095	<b>Status:</b> Ongoing
<b>Title:</b> COG AALL0331, Standard Risk B-precursor Acute Lymphoblastic Leukemia; A Phase III Group-Wide Study		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieuw, MC		
<b>Start - Completion:</b> 15 Dec 2005 - July 2009	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 6 Jun 2007

**Study Objective:** (1) To determine whether the substitution of three intensified phases of post-induction treatment for standard phases will improve the event free survival (EFS) of children with SR-average acute lymphoblastic leukemia (ALL). (2) To determine whether the addition of four doses of PEG Asparaginase, given once every three weeks during consolidation and interim maintenance phases, will improve the EFS for children with SR-low ALL. (3) To identify potentially modifiable factors associated with impaired health related quality of life (HRQOL) at different periods of therapy in the patients who are SR-average enrolled on the standard risk ALL study. (4) To determine the critical time periods when future intervention studies to mitigate adverse HRQOL outcomes should occur. (5) To correlate Day 29 Minimal Residual Disease (MRD) with EFS and Overall Survival (OS). (6) To correlate early marrow response status with Day 29 MRD status. (7) To improve outcome by identifying additional high risk patients by Day 29 MRD for treatment with fully augmented BFM. (8) To examine the relative contributions of genetic factors and early treatment response to outcome by comparing the outcome of patients with and without TEL-AML1 fusion or triple trisomy and low levels of MRD at end Induction who are treated with identical therapy on the standard arms of the SR-low and SR-average trials.

**Technical Approach:** Patients treated on this study will receive multiple drugs all designed to kill leukemia cells. Patients who have an appropriate donor will be given a blood and marrow transplant. Those without an appropriate donor will continue on with more chemotherapy. Patients with high levels of cancer cells in the spinal fluid will also receive radiation to the brain. Boys with leukemia cells in the testes will receive radiation to the testes. Patients receiving a blood and marrow transplant will also be given radiation to the entire body before their transplant and will be hospitalized for about three months during treatment. The new drug for patients with leukemia containing the Philadelphia chromosome positive (Ph+) is called Imatinib (STI571), and it is given throughout treatment. If a patient goes on to have a blood and marrow transplant, Imatinib (STI571) may be given after the transplant at the transplant center or at the primary care center

**Progress:** This greater than minimal risk protocol remains open to enrollment with two subjects enrolled at MAMC, one during the past 12 months. Both subjects continue to receive study treatment.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205105	<b>Status:</b> Terminated
<b>Title:</b> COG-LTF, A Groupwide Process for Collecting Long Term Follow Up Data		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieuw, MC		
<b>Start - Completion:</b> 12 Jul 2005 - indef	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 12 Jun 2007

**Study Objective:** The specific objective is to establish a single mechanism for regular annual local Institutional Review Board (IRB) approval for COG member institutions by aggregating protocols for which only follow-up data collection is needed.

**Technical Approach:** This document is designed to facilitate follow-up data collection for Children's Oncology Group (COG) studies that are closed to accrual and for which all patients in an institution have completed therapy. This includes studies that originated in the Children's Cancer Group (CCG), the Pediatric Oncology Group (POG), the Intergroup Rhabdomyosarcoma Study Group (IRSG), and the National Wilms Tumor Study Group (NWTSG) as well as new COG studies.

**Progress:** During FY07, the Pediatric Hematology/Oncology staff discontinued use of this administrative follow-up tool and requested reactivation of three treatment protocols to continue long term follow-up of patients enrolled under the original studies.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205110	<b>Status:</b> Ongoing
<b>Title:</b> COG AALL03N1, Understanding the Ethnic and Racial Differences in Survival in Children with Acute Lymphoblastic Leukemia		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieuw, MC		
<b>Start - Completion:</b> 17 Nov 2005 - May 2008	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 16 Jul 2007

**Study Objective:** (1) To determine and compare adherence to 6-MP in a cohort of children with ALL from four different ethnic and racial groups (Caucasians, African-Americans, Hispanics, and Asians) receiving maintenance chemotherapy, using the following assessments: serial red cell 6-MP metabolites (6TGN and MethylTIMP), frequency of 6-MP dosing using an electronic pill monitoring system (MEMS®), and self-report of adherence to 6-MP by questionnaire. (2) To determine the impact of adherence to 6-MP (measured using 6TGN, MeTIMP, MEMS® and self-report data independently) on event-free-survival (EFS) in the entire cohort, after adjusting for known predictors of disease outcome. (3) Define a critical level of adherence (measured independently by 6TGN, MeTIMP, MEMS®, self-report) that has a significant impact on EFS for the entire cohort. (4) Describe prevalence of adherence to 6-MP by ethnicity (6TGN, MeTIMP, MEMS®, Selfreport). (5) Describe behavioral and socio-demographic predictors of adherence using the questionnaire data. (6) Describe the pill-taking practices in this cohort using the MEMS® data. (7) To evaluate the impact of adherence on ethnic/racial difference in EFS. (8) To assess the concordance among 6TGN and MeTIMP levels, electronic pill monitoring, and self-reported adherence in the ethnic/racial groups.

**Technical Approach:** This study will assess adherence to 6-MP in a cohort of children with ALL from four different ethnic and racial groups (Caucasians, African-Americans, Hispanics, and Asians), who are receiving maintenance chemotherapy, by measuring red cell 6-MP metabolites (6TGN, MethylTIMP), frequency of 6-MP dosing using an electronic pill monitoring system (MEMS), and self/care-giver report of adherence to 6-MP. Participants will be asked to provide 5 ml blood samples during 7 time points and complete an adherence questionnaire at 4 time points during their regularly scheduled clinic appointments. Blood samples will be used for analysis of genetic polymorphisms related to the efficacy of anti-leukemic therapy, and measurement of red cell 6TGN/TIMP levels (eg. TPMT). Participants will also be given an electronic cap to use with their 6-MP medication bottle that will record the date and time of bottle opening. The COG anticipates about 720 patients less than or equal to 21years of age will be participating in this study. The enrollment for MAMC is estimated to be 2-3 patients per year.

**Progress:** This greater than minimal risk protocol remains open to enrollment with no subjects enrolled to date.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206034	<b>Status:</b> Completed
<b>Title:</b> COG ACNS0423: A Phase II Study of Concurrent Radiation and Temozolomide Followed by Temozolomide and Lomustine (CCNU) in the Treatment of Children with High Grade Glioma		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; COL John B. Halligan, MC; MAJ Kenneth H. Lieu, MC		
<b>Start - Completion:</b> 21 Dec 2005 - Mar 2006	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 30 Nov 2006

**Study Objective:** (1) To determine whether temozolomide given during radiation therapy followed by the combination of Temozolomide and CCNU as adjuvant therapy results in an improvement in event-free survival compared to historical control cohorts. Target tumors are: o Anaplastic Astrocytoma; Glioblastoma Multiforme; Gliosarcoma. (2) To further assess the toxicity of adjuvant treatment with CCNU and temozolomide following XRT and concurrent temozolomide in a larger group of patients.

**Laboratory Correlates:** (1) Investigate MGMT expression in formalin-fixed, paraffin-embedded biopsy specimens of brain tumors using immunohistochemical methods. (2) Identify those tumors in which MGMT expression is silenced by determining promoter CpG methylation in DNA isolated from formalin-fixed, paraffin-embedded tumor samples. (3) Investigate whether a functional MMR system is present in tumor cells by using microsatellite instability assays to compare DNA isolated from formalin-fixed paraffin-embedded tumor samples with DNA isolated from the patient's peripheral blood white cells. (4) Determine p53 expression using standardized immunohistochemical techniques. p53 mutation analysis will incorporate microdissection-based topographic genotyping and direct sequence analysis. (5) Determine MIB-1 indices in tumor samples using standardized immunohistochemical techniques. (6) Determine the frequencies of GSTM1, GSTT1, and GSTP1 allelic variants in patients with high grade glioma. (7) Determine the level of protein expression of GSTP1 in tumor specimens. (8) Determine whether polymorphisms in GSTP1, GSTM1 and GSTT1 genes and tumor GSTP1 protein expression are associated with survival, hypothesizing that patients with inherent low activity GST genotypes and low GSTP1 protein expression will have increased survival time. (9) Assess whether germline polymorphisms of the GST genes are correlated with severity of chemotherapy toxicity, hypothesizing that patients with low activity GST genotypes will have decreased clearance of the metabolites of chemotherapy agents, and thus will have higher degree of toxicity. (10) Characterize allelic imbalance and copy number changes associated with high-grade gliomas by Affymetrix SNP arrays. (11) Characterize gene expression changes associated with high-grade gliomas by Affymetrix U133plus2 arrays. (12) To correlate any identified chromosomal abnormalities and differentially expressed genes with clinical parameters such as age, tumor location, degree of resection, histological grade, p53 expression, progression free survival, overall survival, treatment responses to determine their prognostic significance. (13) Identify oncogenes and tumor suppressor genes involved in the pathogenesis and malignant phenotype of pediatric high grade gliomas.

**Technical Approach:** Patients will be given radiation therapy (RT) to the brain 5 days a week for 6 weeks. Within the first week of starting RT the patient will begin taking Temozolomide orally (90 mg/m<sup>2</sup>/day) and continue taking the drug for 42 days (6 weeks). After completion of RT and the 6-week treatment with Temozolomide, patients will be given no treatment for a 4-week rest period. During Maintenance, patients will take oral Temozolomide again, but this time at a higher dose (160 mg/m<sup>2</sup>/day) for five days in a row followed by a 37 day break. In addition, patients will take another chemotherapy drug known as Lomustine (CCNU) orally with the temozolomide on day 1.

Patients will be treated on this study for about 11-12 months. Expected enrollment for MAMC is 1-2 patients per year.

**Progress:** This protocol was reported as completed in October 2007, with no MAMC subjects enrolled.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206052	<b>Status:</b> Terminated
<b>Title:</b> COG ACNS0331 A Study Evaluating Limited Target Volume Boost Irradiation and Reduced Dose Craniospinal Radiotherapy (18.00 Gy) and Chemotherapy in Children with Newly Diagnosed Standard Risk Medulloblastoma: A Phase III Double Randomized Trial		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Joseph P. Brooks, MC; MAJ Kenneth H. Lieuw, MC		
<b>Start - Completion:</b> 30 Mar 2006 - Oct 2009	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 16 Jan 2007

**Study Objective:** Primary Objective: To determine whether reducing the craniospinal dose of radiation therapy to 18.00 Gy in children 3-7 years of age does not compromise event-free survival and overall survival as compared to treatment with 23.40 Gy of craniospinal radiation; and to determine if reducing the irradiated volume of the primary site tumor boost from the whole posterior fossa to the tumor bed only will not compromise event-free and overall survival.

Secondary Objectives: To evaluate patterns of failure in children treated with an irradiation boost volume smaller than conventional posterior fossa volumes. To reduce the cognitive, auditory and endocrinologic effects of treatment of average-risk medulloblastoma by reducing the dose of craniospinal irradiation therapy. To determine if the audiologic and endocrinologic toxicity will be reduced with the use of limited tumor boost volume irradiation compared to patients treated with conventional target volumes of radiation. To develop an optimal gene expression medulloblastoma outcome predictor, validated prospectively in a multi-institution randomized clinical trial. To improve compliance with long-term quality of life and functional status data submission by educating institutional nurses to administer and submit for analysis a battery of four instruments: Behavior Assessment System for Children (BASC), Adaptive Behavior Assessment System (ABAS), Behavior Rating Inventory of Executive Function (Brief), PedsQLTM 4.0.

**Technical Approach:** In order to compare the effects of different doses and volumes of radiation, children will be randomized to radiation treatment plans at the time of study entry. Children ages 3 and less than age 8 will be randomized twice. They will be randomized between two doses of craniospinal radiation and between a standard volume boost and a smaller volume boost. All children 8 years and older will be given the standard dose of craniospinal radiation and will only be randomized for the boost volume of radiation. Chemoradiotherapy begins about 4 weeks after surgery. Radiation therapy to the brain and spine will be given 5 days each week for 6 weeks. Vincristine will be given IV push once a week for 6 weeks beginning at Week 1 (one week after the start of radiation). Maintenance Chemotherapy begins 4 weeks after the completion of chemoradiotherapy. There will be 9 cycles of maintenance; two different kinds of cycles given. Cycle A lasts for 6 weeks and Cycle B for 4 weeks (given after the completion of 2 A cycles).

**Progress:** This greater than minimal risk protocol remains open to enrollment with no subjects enrolled during FY07. A change in the role of PI from Dr. Lieuw to Dr. Forouhar was approved. No external adverse events have been reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206095	<b>Status:</b> Ongoing
<b>Title:</b> COG AEWS02B1, A Group wide Biology and Banking Study for Ewing Sarcoma		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieuw, MC		
<b>Start - Completion:</b> 26 Jul 2006 - May 2016	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 22 May 2007

**Study Objective:** Objectives: (1) To develop a mechanism to collect and distribute tumor specimens to various investigators, and a system to prioritize and develop quality-control measures for central data reporting of studies undertaken. (2) To determine the prognostic significance of translocation subtype in Ewing sarcoma; to determine the prognostic significance of translocation negative Ewing sarcoma. (3) To determine the prognostic significance of MRD detection in bone marrow specimens by RT-PCR determination of EWS-ETS fusion genes. (3) To determine whether serum levels of IGF1, IGFBP3 are of significance in the outcome of patients with Ewing sarcoma. (4) To determine whether RNA expression profiles performed on diagnostic specimens will allow for the identification of newer prognostic categories and potentially new molecular targets for treatment in Ewing sarcoma. (5) To identify new treatment targets for therapy. Further testing of these potential targets will be carried out in hopes of expediting translation of these findings to the clinic. (6) To establish a bank of Ewing sarcoma xenografts in SCID/Beige mice. (7) To establish clinical proteomics as a resource for investigations of altered signaling molecules in the pathogenesis of Ewing sarcoma.

**Technical Approach:** Study AEWS02B1 is a biology and banking study for Ewing Sarcoma designed to analyze biological factors of Ewing's tumors and relate tumor characteristics to treatment outcomes. At initial diagnosis extra tumor specimens will be sent to the Children's Oncology Group (paraffin blocks or unstained slides and thick sections, blood, bone marrow, serum, fresh sterile tumor frozen in OCT media, and fresh sterile tumor in RPMI). Pathologists are encouraged to submit additional tumor tissue obtained at the time of later biopsies or surgical procedures to document response, recurrence, or progressive disease, and tissue obtained at autopsy. Enrollment for MAMC is estimated to be 1-2 patients per year.

**Progress:** Approved protocol documents were released to the study staff 26 July 2006. One subject enrolled in this biology protocol during FY07. Changes to the protocol included the addition of Dr. Faucette as associate investigator, and a change in the role of PI from Dr. Lieuw to Dr. Forouhar. The study remains open to enrollment.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206096	<b>Status:</b> Ongoing
<b>Title:</b> COG AHOD0431, A Phase III Study for the Treatment of Children and Adolescents with Newly Diagnosed Low Risk Hodgkin Disease		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieuw, MC		
<b>Start - Completion:</b> 11 Aug 2006 - Feb 2009	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 22 May 2007

**Study Objective:** Objectives: (1) To investigate the paradigm of response-based therapy for low risk Hodgkin disease by eliminating involved-field radiation therapy (IFRT) for subjects who achieve a CR with initial chemotherapy. (2) To investigate whether three cycles of AV-PC\* for the treatment of low risk Hodgkin disease is sufficient to induce CR in at least 80% of subjects. (3) To investigate whether subjects who experience a low risk relapse after initial treatment with chemotherapy alone can be successfully treated with a salvage regimen consisting of IV/DECA and IFRT. (3) To maintain the overall survival (OS) for subjects with low risk Hodgkin disease at or above 97%. (4) To determine the prognostic significance of very early response as measured by FDG-PET or gallium after the first course of chemotherapy. (5) To evaluate the prognostic significance of elevation of ESR and CRP at the time of diagnosis in low risk Hodgkin disease on CR rate and relapse rate after chemotherapy alone. (6) To determine the frequency and severity of late effects of therapy including thyroid dysfunction, infertility, cardiotoxicity and second malignant neoplasms.

**Technical Approach:** All patients will have initial treatment utilizing AV-PC\* with or without involved field radiation therapy. Those patients who are in complete remission after three cycles of AV-PC\* will begin follow-up. Those patients who are in partial remission after three cycles will receive involved field radiation therapy. Those who fail to achieve a partial remission with initial chemotherapy, who have progressive disease prior to completing initial therapy, or who fail to achieve a complete remission after radiation therapy will be off study. All patients with a positive FDG-PET (or gallium) prior to initiating treatment will have a second scan after one course of AV-PC\* utilizing the same modality as the initial scan (FDG-PET strongly encouraged if available). Those with a persistently positive study will have a third scan after chemotherapy to document remission status. Patients who experience a biopsy proven low risk recurrence after achieving a complete remission with chemotherapy alone will be treated with a salvage regimen. The initial treatment will consist of 3 cycles of AV-PC\*. Each cycle is 21 days in duration and commences on Day 1 if the ANC > 750 (with patients off G-CSF for at least 2 days) and platelets are > 75,000.

Subjects in complete remission after three courses of initial chemotherapy will stop treatment and begin follow-up. Subjects with partial remission after three courses of initial chemotherapy will proceed to involved field radiation therapy. Radiation therapy will commence approximately 4 weeks after the 3rd cycle of AV-PC\* is completed and when ANC >1000 and platelet count >100,000. Patients who experience a biopsy proven low risk relapse after achieving a complete remission with chemotherapy alone at initial treatment, and therefore have not had prior radiation therapy, will be treated with two cycles of Ifosfamide and Vinorelbine, followed by two cycles of Dexamethasone, Etoposide, Cisplatin, ARA-C followed by involved field radiation therapy. Each cycle will be 21 days in length. All relapses must be biopsy proven. All patients on the salvage regimen will proceed to involved field radiation therapy after four cycles of salvage chemotherapy. Radiation therapy will commence approximately 4 weeks after the 2nd cycle of DECA is completed and when ANC >1000 and platelet count >100,000.



**Progress:** Approved protocol documents were released to the study staff 11August 2006. One subject enrolled during FY07, and continues to receive treatment. Changes to the protocol included Amendment #1, the addition of Dr. Faucette as associate investigator, and a change in the role of PI from Dr. Lieuw to Dr. Forouhar. No serious adverse events have been reported. The study remains open to enrollment.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206097	<b>Status:</b> Ongoing
<b>Title:</b> AREN03B2, Renal Tumors Classification, Biology, and Banking Study		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieuw, MC		
<b>Start - Completion:</b> 26 Jul 2006 - Indef	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 22 May 2007

**Study Objective:** To classify patients with renal tumors by histological categorization, surgical-pathological stage, presence of metastases, age at diagnosis, tumor weight and loss of heterozygosity for chromosomes 1p and 16q, to thereby define eligibility for a series of therapeutic studies. To maintain a biological samples bank to make specimens available to scientists to evaluate additional potential biological prognostic variables and for the conduct of other research by scientists.

**Technical Approach:** This classification protocol will provide the mechanism to identify renal tumor patients on a population basis, and to describe their characteristics at diagnosis. This study will also establish the natural history (relapse-free and overall survival) for patients with disease for which there will not be a therapeutic or outcomes study (all renal tumors except Wilms, rhabdoid, clear cell sarcoma, and renal cell carcinoma). These cases, after central review results are reported back to the enrolling Institution, will be followed (date of last follow-up, relapse, and death) as part of their enrollment on AREN03B2. It is expected that all such patients, even with benign tumor, will be followed at least yearly, for a period of about ten years, by the enrolling Institution (at the time of enrollment, institutions will be notified which cases must be followed). Patients less than 30 years of age will be participating in this study. The enrollment for MAMC is estimated to be 1-2 patients per year.

**Progress:** Approved protocol documents were released to the study staff 26 July 2006. One subject enrolled during FY06, and continues to be followed. Changes to the protocol included Amendment #1, Amendment #2, the addition of Dr. Faucette as associate investigator, and a change in the role of PI from Dr. Lieuw to Dr. Forouhar. No serious adverse events have been reported. The study remains open to enrollment.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207056	<b>Status:</b> Completed
<b>Title:</b> ACNS0223: A Pilot Study Using Carboplatin, Vincristine, and Temozolomide for Children < 10 Years with Progressive/Symptomatic Low-Grade Gliomas		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieuw, MC		
<b>Start - Completion:</b> 5 Mar 2007 - Jul 2008	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** To evaluate the feasibility and toxicity of an induction and maintenance regimen consisting of cycles of carboplatin, vincristine followed with temozolomide in children < 10 years of age with progressive and/or symptomatic low-grade gliomas.

Secondary Objectives are to determine: (1) the response rate in patients treated with the above regimen, (2) the 3 year progression-free-survival and survival of patients with progressive and/or symptomatic low-grade gliomas who are treated with a regimen of carboplatin, vincristine and temozolomide, and to correlate responses and progression-free survival with the genomic profiles of these tumors.

**Technical Approach:** The COG anticipates about 50 patients who are less than 10 years of age will participate in this study, with enrollment at MAMC is estimated to be one to two patients per year.

A diagnostic MRI will be taken within 30 days prior to starting treatment. Progress will then be monitored by further MRIs as the study progresses. Patients will have central venous lines placed through which the chemotherapy will be administered. Carboplatin and vincristine, followed by temozolomide, will be administered both in induction and maintenance. Induction will consist of one cycle of carboplatin/vincristine followed by temozolomide for ten weeks duration. Patients will rest during weeks 7, 8, and 9 of the Induction period when no chemotherapy is given. Induction is followed by maintenance with six 10-week cycles of carboplatin/vincristine with temozolomide. All chemotherapy on this study will be given on an outpatient basis unless side effects develop that require hospitalization.

**Progress:** This protocol received initial approval by the IRB 23 January 2007; however, the study closed enrollment in July 2007 with no subjects enrolled at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207057	<b>Status:</b> Ongoing
<b>Title:</b> Safety and Efficacy of Varicella Zoster Immune Globulin (Human) (VariZIG™) in Patients At-Risk of Varicella Infection		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Loranee E. Braun, MC		
<b>Start - Completion:</b> 19 Apr 2007 - Feb 2010	<b>Funding:</b> None	<b>Periodic Review:</b> 2 Jan 2008

**Study Objective:** The objectives of the expanded access protocol are to outline the handling and use of VariZIG™ which is to be distributed by FFF enterprises under the expanded access protocol (VZ-009), and to collect safety and efficacy data for VariZIG™.

**Technical Approach:** This will be an open-label expanded access protocol to assess the safety and efficacy of VariZIG™ in the prevention or reduction of complications resulting from varicella infections in at-risk patients exposed to individuals with contagious varicella infections. This expanded access protocol is intended to provide VariZIG™ to all patients determined by their physician to be in need of this treatment, and who give their informed consent, until licensing of VariZIG™. Thus, the number of patients to be enrolled under this expanded access protocol is unknown and patients will not be randomized since this study is an open-label design.

Dosing of VariZIG™ is weight based at 125 IU/10 kg body weight to a maximum of 625 IU and minimum of 125 IU for body weight less than 10 kg, administered IM within 96 hours of exposure to VZV. Treatment may be of uncertain value after 96 hours. Repeat dosing of VariZIG™ may be required in the event of subsequent exposure in an at-risk patient 1 month after VariZIG™ administration or if anti-VZV titers are negative.

At visit 1 (day 0), study assessments are performed by the investigator or other designated and qualified healthcare provider and a dose of VariZIG™ based on body weight is administered. Collection of pre-treatment lab data if available. At visit 2 (day 1 to day 4) and visit 3 (between day 7 to 20 or approximate day of varicella rash development if applicable), evaluation of varicella lesions, if applicable, and laboratory assessments and safety assessments are performed. At visit 3 (Between day 7 to 20 or day of varicella rash development if applicable), evaluation of varicella lesions, collection of lab data if available. At visit 4 (day 28 to 42 (closeout) or early termination): clinical review of varicella lesions and infection severity. Return visits at the discretion of the investigator. Laboratory assessments and safety assessments are performed. A log of concomitant medications including transfusions, herbal preparations and prescription and non-prescription medications are kept throughout the study.

Laboratory assessments include the following data if available: hematology assessments: hemoglobin, hematocrit, WBC count and differential, RBC count and platelet count. Blood chemistry: total bilirubin, AST, ALT, alkaline phosphatase, lactate dehydrogenase, creatinine, BUN. Safety assessments are accomplished through monitoring of adverse events (AE), serious adverse events (SAE), adverse drug reactions, and unexpected adverse drug reactions. All adverse events, including those that are not of a serious nature and those that are expected, will be documented by the investigator (or designates) and examined by the investigator for assessment of both severity and causality.

**Progress:** This greater than minimal risk expanded access protocol was initially approved by the IRB on 23 January 2007, and final approval received on 19 April 2007. No patients were identified as needing treatment with VariZIG™ during FY07.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207071	<b>Status:</b> Ongoing
<b>Title:</b> AAML0531; A Phase III Randomized Trial of Gemtuzumab Ozogamicin (Mylotarg®) Combined with Conventional Chemotherapy for De Novo Acute Myeloid Leukemia (AML) in Children, Adolescents, and Young Adults		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; Ms Deborah K. Siler; MAJ Kenneth H. Lieuw, MC; Susan M Burlingame; Kimberly A Fay		
<b>Start - Completion:</b> 9 May 2007 - Oct 2010	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective is to compare the event free survival (EFS) and overall survival (OS) of de novo acute myeloid leukemia (AML) patients randomized between the best current chemotherapy with or without gemtuzumab ozogamicin (GMTZ).

The secondary objectives are to (1) compare the remission induction rates after two courses of the best current induction chemotherapy utilizing cytarabine (10 days), Daunomycin (3 days), and etoposide (5 days) (ADE (10+3+5)) with or without GMTZ for those patients who are eligible for a HLA-matched family donor (MFD) stem cell transplant (SCT) by virtue of their risk classification, to compare disease free survival (DFS) and OS between patients assigned to MFD SCT if a MFD is available, or to chemotherapy if a MFD is not available, (2) determine the outcome of patients with Down syndrome who are 4 years of age or older at diagnosis and treated on this regimen without GMTZ, (3) compare the EFS and OS of de novo AML patients randomized between the best current chemotherapy with or without GMTZ censoring MFD SCT recipients, (4) identify the optimal cutoff of FLT3/ITD (FLT3 internal tandem duplications) allelic ratios to predict patients at high risk for relapse, (5) assess the ability of a second generation flow cytometric assay to predict patients at high risk for relapse during periods of clinical remission, (6) examine whether GMTZ significantly improves EFS and OS in patients with higher CD33 concentrations/intensity, (7) examine whether GMTZ significantly improves CR, EFS and OS in each of the cytogenetic risk groups (High, Intermediate, and Low risk) identified in prior MRC trials, (8) utilize florescence in situ hybridization (FISH) analysis to identify variant patterns among subgroups of patients who demonstrate the same G-banded chromosomal abnormality (e.g., inv(16)/t(16;16), t(8;21), 11q23 abnormality) and to determine whether these variant patterns account for the heterogeneity of responses to therapy, and (9) examine the impact of complex karyotypes (? 3, ? 4, and ? 5 abnormalities) upon OS and EFS in Intermediate risk patients in whom no high risk or low risk cytogenetics abnormalities exist.

**Technical Approach:** Patients will have a physical examination, an Echo, a bone marrow biopsy, and an LP for cell count and be sent to the lab for blood work, radiology for a CT/MRI, general surgery for central venous line placement and may have a biopsy. Patients will be given chemotherapy as an outpatient in 5 stages lasting 6-8 months. The five stages of chemotherapy are: Induction 1, which is chemotherapy given for 10 days followed by 3 weeks of rest (28 days total), Induction 2, which is chemotherapy given for 8 days followed by 3 weeks of rest (28 days total), and Intensification 1, which is chemotherapy given over 5 days followed by 3 weeks of rest (26 days total). At this point the study doctor will decide if the patient gets a stem cell transplant or more chemotherapy. If chemotherapy is given, the patient will proceed to Intensification 2, which is given over 5 days followed by 3 weeks of rest (28 days total) and Intensification 3, which is high dose chemotherapy given for 2 days followed by 5 days of rest, and then 2 more days of chemotherapy. If patients are assigned to Experimental Arm B, gemtuzumab will be added to two stages of treatment therapy; Induction 1 and Intensification 2; however patients assigned to Standard Arm A will not receive gemtuzumab with any of the treatments. All chemotherapy on

this study will be given on an outpatient basis unless side effects develop that require hospitalization. The COG anticipates about 1000 patients who are <1 month to <30 years of age will be participating in this study. Enrollment for MAMC is estimated to be 1 to 2 patients per year.

**Progress:** This greater than minimal risk protocol was initially approved by the IRB on 27 February 2007, and received final approval 9 May 2007. A change in the role of COG PI from Dr. Lieu to Dr. Forouhar was approved 13 June 2007. No subjects enrolled during FY07.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207087	<b>Status:</b> Ongoing
<b>Title:</b> AREN0532, Treatment for Very Low, Low and Standard Risk Favorable Histology Wilms Tumor		
<b>Principal Investigator:</b> MAJ Melissa A. Forouhar, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Kenneth H. Lieuw, MC		
<b>Start - Completion:</b> 4 Jun 2007 - Oct 2016	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective for Very Low Risk Favorable Histology Wilms tumor is to demonstrate that very low risk patients treated by nephrectomy and observation alone will have a 4 year Event Free Survival of greater than or equal to 85% and 4 year Overall Survival of greater than or equal to 95%; very low risk is defined Stage I favorable histology tumors of weight < 550 g with patient age < 2 years at diagnosis.

The objectives for Low Risk Favorable Histology Wilms tumor are to demonstrate that patients with a low risk of recurrence treated with vincristine and Dactinomycin (Regimen EE4A) will have a 4 year Event Free Survival of at least 90% and 4 year Overall Survival of at least 95%; low risk is defined as Stage I favorable histology disease and either greater than or equal to 24 months of age at diagnosis or with tumor weight greater than or equal to 550g, and Stage II favorable histology disease without Loss of Heterozygosity (LOH) of 1p and 16q.

The objectives for Standard Risk Favorable Histology Wilms tumor are to document continued excellent outcome (4 year Event Free Survival greater than or equal to 85% and Overall Survival greater than or equal to 95%) for patients with Stage III favorable histology Wilms Tumor without LOH of 1p and 16q treated with vincristine, Dactinomycin + doxorubicin + radiotherapy (Regimen DD4A).

### Secondary objective(s)

Secondary objectives are to (1) improve the current 4 year Event Free Survival for patients with Stage I and II Favorable Histology Wilms tumor with LOH of 1p and 16q by adding doxorubicin but not radiotherapy (modified Regimen DD4A) to the standard Dactinomycin and vincristine backbone, (2) determine whether the omission of adjuvant therapy increases the incidence of contralateral kidney lesions in very low risk patients treated by nephrectomy and observation only, (3) determine whether the omission of adjuvant therapy increases the incidence of renal failure in the very low risk patients that have metachronous relapse, and (4) monitor the outcomes for these low and standard risk subsets of Favorable Histology Wilms tumors for correlation with biological data generated from the study of the tissues collected from these same cases on AREN03B2.

**Technical Approach:** Children less than two years old will be consented to the Surgery only and Observation arm and will not receive chemotherapy, but will be watched very closely for recurrence with periodic physical exams, urinalysis, blood tests, nuclear tests, CT, X-ray, MRI, and US. Children and adults with Stage I or II Wilms tumor and no LOH change will get standard therapy, which is surgery followed by nineteen weeks of chemotherapy with Vincristine and Dactinomycin, and perhaps radiation therapy. Children and adults with Stage I or II Wilms tumor who have LOH change will get therapy over a period of about 25 weeks with the two standard drugs Vincristine and Dactinomycin plus the drug Doxorubicin. Radiation therapy will not be given. Children and adults with Stage III Wilms tumor who do not have the LOH change will get Vincristine, Dactinomycin, and Doxorubicin for a period of 25 weeks plus radiation therapy. Children and adults with Stage III Wilms tumor who are found to have the LOH change will not

stay on this study. The COG anticipates about 1300 patients who are less than 30 years of age will participate in this study. Enrollment at MAMC is expected to be one or two patients per year.

**Progress:** This greater than minimal risk protocol was initially approved by the IRB on 24 April 2007, and final approval received on 4 June 2007. No subjects were enrolled during FY07.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205065	<b>Status:</b> Ongoing
<b>Title:</b> Staphylococcus Aureus Intestinal Colonization Among Healthy Infants		
<b>Principal Investigator:</b> LTC Dolores M. Gries, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Curtis J. Donskey, M.D.; Michael J. Pultz; CPT Elisa D. O'Hern, MC; Meera R. Iyer, M.D.; Mary L. Myers, MT; Donald Johnson, MD; COL (Ret) Mary P. Fairchok, MD; CPT Tamatha F. Zemzars, MC; MAJ Steven D. Mahlen, MS; CPT Katy J. Gibson, MC		
<b>Start - Completion:</b> 19 Jul 2005 - May 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 24 Apr 2007

**Study Objective:** (1) To perform a prospective survey to examine the incidence and density of *S. aureus* carriage among healthy infants. (2) To evaluate whether infants with increased density of *S. aureus* in stool have increased frequency of environmental and skin contamination. (3) To examine the molecular epidemiology of *S. aureus* isolates among healthy infants and their mothers. (4) To determine the potential for MRSA and other nosocomial pathogens to grow in stool of healthy infants. (5) To determine the incidence of *S. aureus* infection in healthy colonized infants during the first 2 weeks of life.

**Technical Approach:** A 12-month prospective study will be conducted in the MAMC Newborn Unit and Well Child Clinic. Cultures of anterior nares, skin, discarded stool, and environmental surfaces in the room of infants will be obtained. Cultures of the anterior nares of the mother will be obtained. Samples will be analyzed for the presence of MSSA or MRSA. Stool samples will be evaluated for the ability of MRSA and other important nosocomial pathogens to grow in stool specimens. Molecular typing using pulsed-field gel electrophoresis will be performed at the Cleveland VA Medical Center to identify the potential source of the bacteria.

**Progress:** This protocol remains ongoing for new enrollments and follow-up of 40 subjects enrolled. Thus far, the incidence of staph colonization has been found to be at 20%. One case of MRSA has been found and referred to Pediatric Infectious Disease, and investigators are currently quantifying the density of colonization. Investigators are currently performing studies on fresh samples with the assistance of new associate investigator, Michael Pultz. The density of pathogens data will be reviewed in May 2007 after completion of this procedure.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207048	<b>Status:</b> Ongoing
<b>Title:</b> Mupirocin resistance among Staphylococcus aureus isolates at Madigan Army Medical Center		
<b>Principal Investigator:</b> CPT Jacob S Hogue, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL (Ret) Mary P. Fairchok, MD; MAJ Loranee E. Braun, MC		
<b>Start - Completion:</b> 22 Jan 2007 - Jan 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 2 Jan 2008

**Study Objective:** The objectives of this study are (A) To determine the proportion of methicillin resistant and methicillin sensitive Staphylococcus aureus (MRSA and MSSA, respectively) isolates from pediatric and adult patients obtained during clinical practice in the MAMC Microbiology laboratory that are resistant to mupirocin (an antibiotic used topically under the trade name Bactroban™), (B) to evaluate the change in mupirocin resistance rates and patterns for newly isolated MRSA at MAMC over a one year period, and (C) to correlate the occurrence of resistance to mupirocin with its use in MRSA infection control and MSSA colonization.

**Technical Approach:** We will be performing an observational study investigating the prevalence of mupirocin resistance over a 12 month prospective period and a 6 month retrospective period among Staphylococcus aureus isolates at MAMC. S. aureus specimens isolated in the MAMC Clinical Microbiology Laboratory will be tested for mupirocin resistance by detecting the plasmid-encoded ileS-2 by PCR in addition to determining the Minimum Inhibitory Concentration (MIC) by E-test. Routine antibiotic susceptibility and characterization of S. aureus isolates as community acquired or nosocomially acquired MRSA will also be performed as needed. A chart review will be performed to document patient age, type of infection, previous use of mupirocin or other antibiotics, household contact with prior mupirocin use, and prior use of a MRSA eradication regimen. In addition, prescription rates for mupirocin will be obtained for the periods relating to the S. aureus isolates for evaluation of clinical utility of mupirocin in the infection control of MRSA.

**Progress:** This minimal risk protocol was approved by the Expedited Review Committee on 22 January 2007. No changes to the protocol have been submitted except for an update of technical staff support. A progress report has not yet been requested.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206021	<b>Status:</b> Completed
<b>Title:</b> EKG Screening in ROTC Cadets; Is It Useful?		
<b>Principal Investigator:</b> CPT Erik R. Johnson, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Mark J. Devenport, MC; COL Robert A. Puntel, MC; LTC Telita D. Crosland, MC; LTC Victoria W. Cartwright, MC; MAJ John A. Edwards, MC; CPT Kirk N. Liesemer, MC		
<b>Start - Completion:</b> 30 Nov 2005 - Jul 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 3 Apr 2007

**Study Objective:** (1) To determine how often screening electrocardiograms (EKG's) in ROTC cadets disclose abnormal EKG findings, (2) which specific cardiac abnormalities are discovered, (3) what percentage of abnormal screening EKG's disclosed life-threatening or serious cardiac illness that require further consultation and (4) what percentage of cadets are disqualified from entering flight school due to EKG findings and/or further evaluation.

**Technical Approach:** This is a retrospective study designed to have no impact whatsoever on the routine care of the ROTC candidates seen at Ft. Lewis, Washington during the Summer of 2005 as part of Warrior Forge. Each year, approximately 500-700 cadets undergo evaluation for flight status as an additional part of their ROTC experience (current year's estimate is around 600) and receive screening EKGs in addition to other routine medical evaluations. Data [age, sex, height, weight, abnormalities listed on EKG, any consultations or further evaluations made, specifically cardiology referral (yes/no and descriptive clinical findings of referral)] will be obtained and recorded into an Excel spreadsheet database using medical records available (CHCS, ICDB, and Aviation Medicine Clinic medical records available for review). Results of each cadet's flight status (yes/no) will be requested from Aviation Medicine Clinic.

**Progress:** This protocol was completed in FY 2007. The initial abstract of findings for this protocol was submitted to USPS, but not accepted. Investigators reviewed the next summer's RPTC EKG records to add more numbers to the data, but that abstract was also rejected. A copy of the final abstract remains pending at the time of this report.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203119	<b>Status:</b> Completed
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**Title:** Alternating Antipyretics: Antipyretic Efficacy Of Acetaminophen Versus Acetaminophen Alternated With Ibuprofen In Children

**Principal Investigator:** CPT Lynne C. Kramer, MC

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** COL (Ret) Mary P. Fairchok, MD; COL (Ret) Patrick C. Kelly, D.O.; CPT Amy M. Thompson, MC; CPT Peaches A. Richards, MC; CPT Keith R. Compton, MC; CPT David P. Harper, MC

**Start - Completion:**

27 Feb 2004 - Feb 2004

**Funding:**

American Academy of Pediatrics via The Geneva Foundation

**Periodic Review:**

22 Aug 2006

**Study Objective:** To compare the antipyretic efficacy of alternating ibuprofen and acetaminophen to acetaminophen alone.

**Technical Approach:** Infants and children 6 months to 6 years meeting inclusion and exclusion criteria who present to the pediatric clinic with a fever of 100.4 or greater will be offered enrollment into the study. Baseline temperature will be recorded and initial dose of acetaminophen will be given. All temperature measurements will be made using a standard oral or rectal thermometer provided by the investigators. Parents will receive a handout and instruction on facts and myths related to fever and fever control in children. Baseline demographic data will be recorded to include age, sex, race, and underlying medical conditions. Parents or caregivers will be trained to take temperature with the study thermometer and administer study medications. Subjects will be randomized via computer based random number to either the acetaminophen group or the acetaminophen/ ibuprofen group. Group selection will be unblinded only to the co-investigator entering the study medications into CHCS. Study medications will include acetaminophen, ibuprofen, and placebos designed to mimic ibuprofen and acetaminophen. Each patient will receive a study medication or placebo at time zero, 3 hours and 4 hours. Acetaminophen group will receive acetaminophen time zero, placebo time 3 hours and acetaminophen time 4 hours. Acetaminophen + ibuprofen group will receive acetaminophen time zero, ibuprofen time 3 hours and placebo time 4 hours.

Temperatures will be obtained and recorded from each subject at 0, 3, 4, 5 and 6 hours. The study will end at 6 hours. All subjects will receive standard of care for their presenting complaints. The study will not interfere with the evaluation or treatment of these complaints. Once the medical evaluation for the presenting complaint is complete subjects will be sent home or admitted depending on their medical condition. For subjects at home, the parent or caretaker will complete the study. A study investigator will contact the parent or caretaker at 6 hours and obtain the results. At the conclusion of the study period, parents will read the provided instruction sheet on what further antipyretics and antipyretic schedule may be administered to the child in the case of continuing fever. The information will be provided as a sealed instruction sheet matched to the randomized group, so that the study investigator will remain blinded.

**Progress:** This protocol was reported as completed in FY07. The study closed enrollment in FY06, with 38 subjects enrolled. Data analysis was conducted and an abstract and manuscript submitted to Pediatrics, which was accepted with minor revisions. There were no statistically significant differences in temperature between the two groups at times 0, 3, 4, and 6 hours. However, subjects in the alternating group had significantly lower mean temperature at five hours ( $p=0.0032$ ). There was no difference in side effects. Parents did not perceive any difference in fever control between the groups. An alternating regimen of acetaminophen with ibuprofen did significantly decrease fever at 5 hours when compared to acetaminophen alone. However the difference was modest and

did not last more than an hour. Parents did not perceive a difference in efficacy. These results lend support for not routinely advocating use of alternating antipyretic schedules. Education of parents about fever phobia may be more beneficial than emphasizing antipyretics. Use of acetaminophen alone appears to be efficacious for control of fever in children when warranted.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 94092	<b>Status:</b> Completed
<b>Title:</b> POG 9351/CCG 7921: Trial of Doxorubicin, Cisplatin, and Methotrexate With and Without Ifosfamide, With and Without Muramyl Tripeptide Phosphatidyl Ethanolamine (MTP-PE) for Treatment of Osteogenic Sarcoma		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieu, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 21 Apr 1995 - Indef	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 21 Mar 2006

**Study Objective:** (1) To improve the survival of patients with osteogenic sarcoma, (2) To compare the results of a prospective, randomized trial of two chemotherapeutic regimens in the treatment of osteogenic sarcoma, (3) To compare the results of a combined chemotherapeutic regimen (high-dose methotrexate, cisplatin, and doxorubicin) given pre-operatively and post-operatively to a similar regimen using the same drugs and adding ifosfamide, (4) To test whether the early introduction of ifosfamide results in a higher rate of good histologic response at the time of definitive surgery, (5) To determine whether histologic response assessed after longer pre-operative chemotherapy with more drugs predicts disease-free survival with the same power as observed in CCG-782 which used a shorter period of pre-operative chemotherapy and fewer drugs, (6) To determine whether liposomal muramyl tripeptide-phosphatidyl ethanolamine (MTP-PE, CGP 19835a), a stimulator of macrophage function, can improve disease-free survival for patients with osteogenic sarcoma, (7) To determine whether multiple drug resistance gene-encoded P-glycoprotein expression is useful for determine prognosis or assigning therapy.

**Technical Approach:** This study is a phase III, prospective, randomized trial of two chemotherapy regimens for the treatment of newly diagnosed, previously untreated osteogenic sarcoma. One regimen calls for the administration of high-dose methotrexate, doxorubicin, and cisplatin. The other regimen calls for the administration of these agents plus ifosfamide. Chemotherapy is administered for 10 weeks prior to surgical resection of the primary tumor and any metastatic disease (CCG patients). Patients also are randomly assigned either to receive muramyl tripeptide (MTP-PE) with maintenance chemotherapy or to receive maintenance chemotherapy alone.

**Progress:** This protocol was permanently closed by COG in April 2007, discontinuing long term follow-up reporting requirements. The protocol closed enrollment in November 1997, with two subjects enrolled. One subject discontinued therapy early and the other subject had continued to be followed at MAMC during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07			<b>Number:</b> 96097			<b>Status:</b> Completed		
<b>Title:</b> POG 9440: National Wilms Tumor Study - 5: Therapeutic Trial and Biology Study								
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC								
<b>Department:</b> Pediatrics						<b>Facility:</b> MAMC		
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC								
<b>Start - Completion:</b> 19 Apr 1996 - Indef			<b>Funding:</b> COG/POG via The Geneva Foundation			<b>Periodic Review:</b> 15 Mar 2007		

**Study Objective:** (1) To increase the survival rate of children with favorable histology Wilms tumor and other renal tumors of childhood, (2) to determine if loss of heterozygosity for chromosome 16q markers in tumor tissue is associated with a poorer prognosis for children with favorable histology Wilms tumor, (3) to determine if loss of heterozygosity for chromosome 1p markers in tumor tissue is associated with a poorer prognosis for children with favorable histology Wilms tumor, (4) to determine if increased DNA content in tumor cells is associated with a poorer prognosis, (5) to decrease the acute and long term morbidity of treatment of children with Wilms tumor, (6) to improve the survival of patients with unfavorable histology tumors including Wilms tumor with diffuse anaplasia and clear cell sarcoma of the kidney by using a new treatment regimen that includes etoposide and cyclophosphamide, (7) to improve survival of patients with malignant rhabdoid tumor of the kidney, (8) to study biology and pathology of patients who present with bilateral Wilms tumor, (9) to conduct hypothesis-driven trials led by diagnostic radiologists in order to develop guidelines, and (10) to establish a biological samples bank containing touch preparations, paraffin blocks, frozen tumor, normal kidney tissue, and serum and urine.

**Technical Approach:** This proposed therapeutic trial involves a number of experimental regimens that are designed either to reduce treatment for the subgroup of patients with the most favorable prognosis, or to intensify treatment for several subgroups with the least favorable prognosis. Patients will be stratified into the appropriate treatment regimens by age, size of tumor at diagnosis and staging of the tumor (Stages 1-V) with favorable/unfavorable histology, including rhabdoid, clear cell sarcomas and Wilms tumor with diffuse or focal anaplasia. Treatment will include nephrectomy or surgical debulking of tumor, radiation therapy to abdomen and/or lungs, and appropriate chemotherapy regimens.

**Progress:** This protocol closed enrollment in June 2002, with two subjects enrolled who continued to be followed at MAMC during FY07. No adverse events or changes to the protocol were reported.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206051	<b>Status:</b> Terminated
<b>Title:</b> ANBL0032 Phase III Randomized Study Of Chimeric Antibody 14.18 (Ch14.18) In High Risk Neuroblastoma Following Myeloablative Therapy And Autologous Stem Cell Rescue		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 6 Apr 2006 - Oct 2006	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 16 Jan 2007

**Study Objective:** Primary objective to determine if monoclonal antibody Chl4.18 + cytokines + isotretinoin (13-cis-retinoic acid, or RA) improves event free survival after myeloablative therapy and stem cell rescue as compared to RA alone, in high risk neuroblastoma patients who have achieved a pre-ASCT response of CR, VGPR, or PR.

Secondary objectives: (1) to determine if monoclonal antibody Chl4.18 + cytokines + isotretinoin (13-cis-retinoic acid, or RA) improves overall survival after myeloablative therapy and stem cell rescue as compared to RA alone, in high risk neuroblastoma patients who have achieved a pre-ASCT response of CR, VGPR, or PR. (2) Determine if immunotherapy + RA improve event free survival and overall survival as compared to RA alone, in the subgroup of high risk INSS stage 4 neuroblastoma patients who have achieved a pre-ASCT response of CR, VGPR, or PR. (3) To determine the variability of 13-cis-retinoic-acid pharmacokinetics and relationship to pharmacogenomic parameters and determine if these levels and/or genetic variations correlate with EFS or systemic toxicity. (4) In the subgroup of neuroblastoma patients who have achieved a pre-ASCT response of CR, VGPR, or PR, determine if there is a difference between the two randomized regimens in reducing the minimal residual disease (MRD) burden as detected by the following parameters: meta-iodobenzylguanidine (MIBG) scan, immunocytology (IC) of blood and bone marrow samples, RT-PCR for tyrosine hydroxylase, PGP 9.5, and MAGE-1 in blood and bone marrow. (5) Determine if change from baseline of MRD as measured by above parameters is associated with event free and overall survival. (6) Determine whether tumor biology at diagnosis correlates with event-free and overall survival, for either of the randomized regimens. (7) Determine the toxicities of the combination of monoclonal Ch14.18 with cytokines. (8) To explore the relationship between antibody-dependent cellular cytotoxicity (ADCC) and EFS. (9) To determine a descriptive profile of human anti-chimeric antibody (HACA) during immunotherapy. (10) To compare the outcome data of the patients with persistent disease documented by biopsy (stratum 07) to the historical data for the analogous patients from CCG-3981.

**Technical Approach:** Patients will be enrolled and randomized into regimen A or B on day 50 post-ASCT, up to day 77 (see special exemption) post-ASCT when 1) total absolute phagocyte count (APC) is at least 1000/?L 2) organ functions have met the eligibility criteria, and, 3) tumor assessment has been completed following the end of radiotherapy at least 5 days before. Randomization will be stratified by pre-ASCT CR versus VGPR versus PR and by purging vs. nonpurging of the stem cells for ASCT. Regimen A consists of oral intake of isotretinoin (13-cis-retinoic acid, or RA) starting day 66 post-ASCT at 80 mg/m<sup>2</sup>/dose twice a day for 14 days every 28 days, for 6 courses. For regimen B, patients will receive oral isotretinoin (13-cis-retinoic acid, or RA) as in regimen A. In addition, patients will receive 5 courses of ch14.18 + cytokines, with ch14.18 + GM-CSF administered in courses 1, 3, and 5, and ch14.18 + aldesleukin (IL-2) given in courses 2 and 4. The intervals between antibody administrations are 28 days for all courses.

**Progress:** This protocol was terminated in January 2007, with no subjects enrolled as study staff decided they would not be able to support the protocol.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204040	<b>Status:</b> Ongoing
<b>Title:</b> National Cystic Fibrosis Foundation Patient Data Registry		
<b>Principal Investigator:</b> COL (Ret) Donald R. Moffitt, MD		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Dana A. Winter, C.R.T.		
<b>Start - Completion:</b> 6 Feb 2004 - Indef	<b>Funding:</b> DCI	<b>Periodic Review:</b> 19 Jan 2007

**Study Objective:** (1) Monitoring epidemiologic trends in the population for CF patients in the US through data collection and entry into the NCF Foundation Patient Registry. (2) Assist in development of therapeutic advances responsible for the improved survival of cystic fibrosis patients.

**Technical Approach:** The CF Patient Data Registry will include patients with cystic fibrosis who are cared for at CF Care Centers throughout the U.S. Locally, this project will include patients from the CF Care Center at Madigan Army Medical Center, which currently cares for 27 CF patients. When a patient and/or parent gives written consent to be included in the registry, updates of the patient's medical information will be sent to the CF National Patient Registry. The information that is sent to the National Patient Registry includes patient name, date of birth, social security number, and zip code of residence. Personal identifiers allow the CF National Patient Registry to track information for patients who receive care at more than one CF center or who move between CF centers. Patients have the choice of participating in the registry without sending the patient's social security number to the CF National Patient Registry. Other information that is sent to the CF National Patient Registry includes the following: specifics of diagnosis (e.g., diagnosis date, sweat test results, genotype); clinical status (e.g., presence of complications, transplant status); test results (e.g., pulmonary function tests, microbiology cultures); nutritional status (e.g., height, weight, nutritional supplements, pancreatic enzyme use); treatment information (e.g., hospitalizations, home therapies, use of new therapies); participation in clinical trials; and demographic data (e.g., educational status, marital status, employment status, and insurance coverage).

**Progress:** This database protocol remains open to enrollment with 21 subjects enrolled. Data continues to be gathered from routine lab follow-up visits and submitted to the CF Foundation, with the patient/parent's permission. No special studies or treatments are prescribed under this protocol.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203046	<b>Status:</b> Ongoing
<b>Title:</b> Telemedicine Based Ultrasound for Detecting Neonatal Heart Disease in Babies at Remote Military or Native American Health Care Facilities		
<b>Principal Investigator:</b> COL Robert A. Puntel, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL James B. Kinney, MC; COL David T. Estroff, MC; David J. Sahn, MD; COL (Ret) Edward R. Carter, MD; Mark D. Reller, MD		
<b>Start - Completion:</b> 22 Jul 2003 - Dec 2006	<b>Funding:</b> DCI via Grant	<b>Periodic Review:</b> 27 Feb 2007

**Study Objective:** This impact and outcomes research proposal will specifically test the hypothesis that a method for reliable and rapid assessment of newborn infants at risk for heart disease can be developed for telediagnosis using a small hand-held ultrasound system with an appropriate high frequency transducer. The unique setting will be that the healthcare professional performing the examination may not be a cardiologist or a fully trained echocardiographer, but the examination will be monitored, supervised and guided using telemedicine links which will also allow control of the scanning system settings by the remote supervisor who is an expert Pediatric Cardiologist/echocardiographer.

The program will assess diagnostic accuracy as the primary outcome variable and time to diagnosis, incidence of unnecessary transport and length of stay during initial hospitalization including transfer when it occurs, as secondary medical outcomes. Diagnosis will be established by testing at a referral center or examination and ultrasound performed by the expert consultant on a follow-up visit occurring at the referral site. In addition to any diagnostic findings of significance which are missed, we will survey and document adverse events in the patient's subsequent course, both medical and social (e.g: parent/baby separation, parental anxiety). Each infant will be followed for 3 months from the time of the initial diagnosis encounter and will be compared to historical controls. Finally, our study will also include a financial outcomes/cost analysis.

**Technical Approach:** This is a prospective, non-randomized, case-control study with measurements obtained at baseline (entry into the study) and three months later. Source data will consist of ultrasound images of the heart transmitted electronically from a remote site to a medical center where they will be read and interpreted. Non-transmitted U/S images and data abstracted from the infant's medical record will be recorded. Data will be obtained at baseline and three months following baseline.

Recruitment and training of health care professionals: two individuals - a pediatrician, family practitioner or obstetrical nurse from each designated participating center will be identified. Initial training in the use of handheld ultrasound systems will occur at MAMC by Drs. Kinney and Puntel and will consist of 2 days of classroom and individual hands-on instruction. A primer on ultrasound instrumentation and methods for performance of cardiac ultrasound will be prepared by Drs. Sahn, Kinney and Puntel. Infants whose families consent will be examined by the attending pediatric cardiologist and have hands-on scanning performed by the trainees under his supervision as the infant's condition allows.

When the portable scanner becomes available for each center and the Telemedicine link is installed and activated, one of the four pediatric cardiologists staffing this program will visit with the trainees at each institution to bring the scanner and operate the telemedicine link, see patients and observe the trainees performing ultrasound examinations, especially in newborns. They will certify on that examination and/or by follow-up observation of Telemedicine observed studies by those healthcare provider-trainees when they are qualified to activate their site and enroll

patients.

Enrollment of patients will begin when all training has been completed and each center has completed its own IRB process. Other care of and testing of the infant will be performed as necessary by the hospital staff and results will be extracted from the patient's medical record. Physical examination, EKG, and/or X-ray will be used, as routinely in a neonatal setting, for identification of potential signs, symptoms, physical examination findings, EKG or radiologic findings of congenital heart disease. Cyanosis will be detected by saturation meter and/or blood gases as necessary. These are part of routine Level II nursery care for newborn infants and will not be altered by the study. These protocols and methods may be specific to the site and documented in the approval of these sites as level 2 or level 3 nurseries.

**Progress:** As of 11/8/2007: A total of 53 separate subjects enrolled in the study; 5 subjects enrolled at Bassett during FY07. Cardiac abnormalities such as PFO, ASD, VSD, and PDA were recognized by TeleEcho and confirmed 100% with follow-up conventional echocardiography.

All active sites have at least one trained provider and the equipment necessary to perform TeleEchos. All sites, except Yukon, have received the necessary medical equipment for the study and upgraded SonoSites are being exchanged as per CRDA.

Currently Madigan, Bassett, Weed, Alaska Native, Elmendorf, Oak Harbor, Bremerton, 3MDG, and Bayne-Jones have received initial IRB approval and/or continuing approval for 2007. Blanchfield will resubmit to the IRB once a new PI completes all requirements. HSRRB has begun the process of reviewing all IRB approved protocols. Madigan, Bassett, Weed, and Alaska Native have received HSRRB approval and/or continuing review. HSRRB approval on Oak Harbor and Bremerton was received 16 November 2007, and Bayne-Jones is expected soon. Investigators await HSRRB final authorization before enrolling subjects at remaining sites. Yukon is still on hold due to staff constraints.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204028	<b>Status:</b> Expired
<b>Title:</b> Pediatric Intubation Training Utilizing the Ferret (mustela putorius furo) Model		
<b>Principal Investigator:</b> COL Robert A. Puntel, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Catherine Kimball-Eayrs, MC		
<b>Start - Completion:</b> 17 Dec 2003 - Dec 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8 Nov 2006

**Study Objective:** This is a training protocol using a ferret model to teach physicians and other health care professions how to endotracheally intubate (i.e. place a plastic tube in the windpipe) neonates and infants. The training is part of a two-day course in pediatric life-saving techniques; the class is called Pediatric Advanced Life Support (PALS) and is developed by the American Heart Association. PALS is offered through the Department of Emergency Medicine two to four times a year.

**Technical Approach:** Students will complete classroom instruction in principles and techniques of pediatric life support. The students will then practice techniques, include endotracheal intubation, on mannequins. Following this practice, students will intubate an anesthetized ferret, which more closely simulates the respiratory anatomy and reflexes of a human child than does a mannequin. Up to six ferrets will be used for each training session and each ferret will serve to train four physicians or other health care providers. The ferrets will be fully anesthetized and will experience no pain during the procedure; they will be closely monitored and observed by a member of the veterinary staff. During the procedure, each of the course participants will learn to place a small plastic tube through the mouth and into the trachea (windpipe) of an anesthetized ferret with the assistance of a small, lighted metal blade called a laryngoscope. The investigators, other course instructors, and veterinary staff will directly supervise the procedure. If any ferret is traumatized or shows signs of problems with the anesthetic drugs, the procedure will be stopped on that animal. No animal will undergo more than seven intubation attempts. After the training session is complete, the animals will be allowed to wake up from anesthesia and will be returned to their usual housing at the MAMC Animal Facility. In the first days following the procedure, the ferrets may experience a mild sore throat, and they will be offered moist food as needed. Ferrets will be housed and maintained according to standard animal husbandry protocols.

**Progress:** Four PALS courses were held in FY 2006 with 88 medical personnel successfully trained using many simulators and 10 ferrets for tracheal intubation training. With the new SimBaby model, ferret use is less than in previous years. Expect to eventually phase out use of live animals due to the quality of simulation trainers becoming available. Four labs are planned for FY 2007. This protocol provided training for 91 medical personnel in three training labs. Due to changes in PALS certification only MDs will be trained in the future with one lab per year. This protocol will be phased out due to the development of adequate simulation training models.

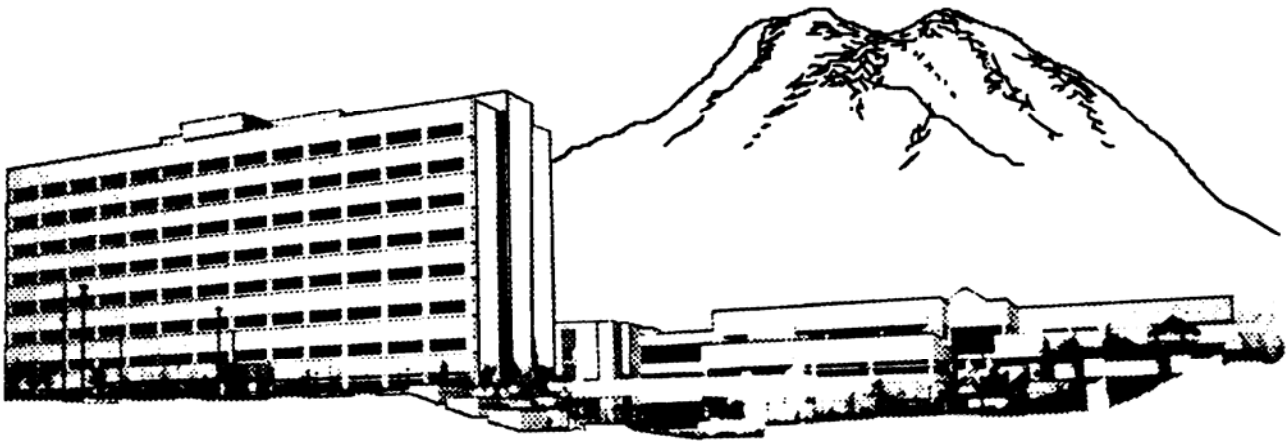
### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207044	<b>Status:</b> Ongoing
<b>Title:</b> Pediatric Intubation Training Utilizing the Ferret (mustela putorius furo) Model		
<b>Principal Investigator:</b> COL Robert A. Puntel, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Catherine Kimball-Eayrs, MC		
<b>Start - Completion:</b> 10 Jan 2007 - Jan 2010	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** This is a training protocol rather than an experimental protocol. The goal of the protocol is to improve the training of physicians and other health care providers in pediatric endotracheal intubation, thereby improving the outcome of pediatric patients whom they treat.

**Technical Approach:** This is a training protocol using a ferret model to teach physicians and other health care professionals how to endotracheally intubate (i.e. place a plastic tube in the windpipe) neonates and infants. This training is part of a two-day course in pediatric life-saving techniques; the class is called Pediatric Advanced Life Support (PALS) and is developed by the American Heart Association. PALS is offered through the Department of Emergency Medicine two to four times a year. Students will complete classroom instruction in principles and techniques of pediatric life support. The students will then practice techniques, include endotracheal intubation, on mannequins and SimBaby (computerized mannequin). Following this practice, students will intubate an anesthetized ferret, which more closely simulates the respiratory anatomy and reflexes of a human child than does a mannequin. Up to six ferrets will be used for each training session and each ferret will serve to train up to six physicians or other health care providers. The ferrets will be fully anesthetized and will experience no pain during the procedure; they will be closely monitored and observed by a member of the veterinary staff. During the procedure, each of the course participants will learn to place a small plastic tube through the mouth and into the trachea (windpipe) of an anesthetized ferret with the assistance of a small, lighted metal blade called a laryngoscope. The investigators, other course instructors, and veterinary staff will directly supervise the procedure. If any ferret is traumatized or shows signs of problems with the anesthetic drugs, the procedure will be stopped on that animal. No animal will undergo more than seven intubation attempts. After the training session is complete, the animals will be allowed to wake up from anesthesia and will be returned to their usual housing at the MAMC Animal Facility. In the first days following the procedure, the ferrets may experience a mild sore throat, and they will be offered moist food as needed. Ferrets will be housed and maintained according to standard animal husbandry protocols.

**Progress:** Approved protocol 10Jan2007. This protocol provided training for 91 medical personnel in three training labs. Due to changes in PALS certification only MDs will be trained in the future with one lab per year. This protocol will be phased out due to the development of adequate simulation training models.



## **Detail Summary Sheets**

Department of Preventive Medicine

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207064	<b>Status:</b> Completed
<b>Title:</b> Hearing Loss in U.S. Army Aviators, Comparing 2005 to 2001		
<b>Principal Investigator:</b> MAJ Douglas A. Badzik, MC		
<b>Department:</b> Preventive Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Andrew R. Wiesen, MC; William E. Daniell, M.D., MPH; LTC Stephen A. Burnstein, MD, MC		
<b>Start - Completion:</b> 26 Feb 2007 - Apr 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objectives of this study are to (1) establish a peace-time (defined as prior to 2002 and the current war on terrorism, with combat operations in Iraq and Afghanistan) baseline of audiometric health for U.S. Army aviators as a function the prevalence and degree of significant threshold shifts, by evaluating audiograms of individual aviators from calendar year 2001 against their baseline audiogram obtained at entry into aviation, (2) determine the war-time (defined as calendar years 2002-2005 to include the current war on terrorism, with combat operations in Iraq and Afghanistan) audiometric health for U.S. Army aviators as a function the prevalence and degree of significant threshold shifts, by evaluating audiograms of individual aviators from calendar year 2005 against their baseline audiogram obtained at entry into aviation, (3) compare audiometric health of U.S. Army aviators in peace-time and war-time environments, adjusting for total hours flown as a measure of noise exposure, and (4) evaluate peace and war time audiometric health of Army aviators for evidence of differences between various aircraft comparing AH-64 (Apache), UH-60 (Blackhawk), CH-47 (Chinook), OH-58 (Kiowa Warrior) and fixed wing aircraft.

**Technical Approach:** This proposal aims to use a retrospective cohort study to evaluate the audiometric health, as a function of the prevalence of significant threshold shifts, of U.S. Army aviators exposed to a war-time environment (defined as calendar years 2002-2005 to include the current war on terrorism, with combat operations in Iraq and Afghanistan). Audiograms from individual aviator's annual flight physicals from calendar year 2005 will be compared against their baseline audiograms obtain at entry into flight school and evaluated for evidence of threshold shift as defined but the Army's hearing conservation program which defines a significant threshold shift as a change of 15 dB at any frequency 1000-4000 Hz in either ear and/or a 10 dB change or more in the average hearing threshold at 2,000-4,000 Hz in either ear. The unexposed group will be U.S. Army aviators who have been exposed only to a peace-time environment (defined as prior to 2002 and the current war on terrorism, with combat operations in Iraq and Afghanistan). Audiograms from these individual aviators's annual flight physical from calendar year 2001 will be compared against their baseline audiograms obtain at entry into flight school and evaluated for evidence of threshold shift. The prevalence and degree of significant threshold shift seen in the exposed aviators (war-time) will be compared those of the unexposed aviators (peace-time). Data to be used in this study is preexisting and is located at US Army Aeromedical Activity (USAAMA) center, at Fort Rucker. Protected health information is limited to social security numbers which identifies each subject's data; however, the data will be de-identified prior to the data being removed from USAAMA for analysis. Analysis of the data will involve use of logistic regression. The risk to the study subject is none, in that preexisting data will be used. The benefit the subject and to US Army aviators in general is to identify ways to improve hearing conservation in Army aviators. Support will be provided by Dr. William Daniell, University of Washington and LTC Andrew Wiesen, MAMC, both of whom are part of my Masters Thesis committee. Additional support will come from LTC Stephen Bernstein, Director of USAAMA.

**Progress:** This protocol was reported as completed in June 2007. Data analyzed from a 3,802 U.S. Army (USA) aviators on active flight status. The prevalence of significant threshold shift (STS) in the 2001 cohort by OSHA and USA criteria was 6.1% and 13.7% respectively compared to 11.6%

and 23.8% for the 2005 cohort. Using logistic regression it was determined that the 2005 cohort was about 2.5 times as likely to have a STS compared to the 2001 cohort.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207033	<b>Status:</b> Ongoing
<b>Title:</b> Impact of the DoD Paradigm Shift on VA Amputee Care		
<b>Principal Investigator:</b> CPT Kristin E. Erickson, MC		
<b>Department:</b> Preventive Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Christopher T. Littell, MC; Gayle E. Reiber, DO, MPH; Douglas G. Smith, MD; Lynne V. McFarland, MS, PhD; Charles Maynard, PhD		
<b>Start - Completion:</b> 19 Dec 2006 - Dec 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 11 Dec 2007

**Study Objective:** To capture, at one-year post-amputation, the current utilization and cost of prostheses for amputees with major amputations returning from Operation Enduring Freedom/Operation Iraqi Freedom. To then project 5, 10, 20 and 30-year utilization and cost of prostheses and assistive devices using three different scenarios: outsourced community fair-market costs, outsourced discounted Medicare costs and VA in-house fabrication costs with direct purchase of components and assembly by skilled prosthetists.

**Technical Approach:** Background/Rationale: A recent Department of Defense (DoD) Rehabilitation Directive aims to return amputees from Operation Enduring Freedom and Operation Iraqi Freedom (OEF/OIF) to pre-injury function and provide the option of returning to active duty. To meet this goal, Walter Reed and Brooke Army Medical Center Rehabilitation Centers offer state-of-the-art rehabilitation care and prosthetic devices. Current state-of-the-art prosthetic technology is approximately six times more expensive than prosthetic technology used in 2000. The VA wants to be prepared to provide the prostheses and services needed by amputees being discharged from DoD.

**Objectives:** To provide clinicians and policy-makers information on changes in prosthetic utilization patterns, projected costs, amputee satisfaction, prosthetic procurement alternatives and expert recommendations to guide future prosthesis-related personnel, laboratory and economic decisions.

**Aim.** To capture, at one-year post-amputation, the current utilization and cost of prosthetic devices for amputees with major amputations returning from Operation Enduring Freedom/Operation Iraqi Freedom. To then project 5-year, 10-year, 20-year and lifetime utilization and cost using three different payment scenarios: outsource and community rates, Medicare rates, or in-house VA rates.

**Methods:**

**Research Plan:** Survey of all OEF/OIF amputees one year post-initial-amputation. Data will be used to generate economic models to forecast cost over 5-, 10-, 20-year and lifetime of the amputees.

**Principal Sources of Data:** DoD Amputee Database. Data on prosthetic satisfaction will be collected with surveys of amputees from Operation Enduring Freedom and Operation Iraqi Freedom. Data for trends of prosthetic utilization will be evaluated by a panel of experts on rehabilitation and prosthetic devices.

**Principal Type of Analysis:** Markov models with a finite number of states for the economic assessments comparing projected prosthetic use by the three methods of procurement (prosthetics engineered by VA prosthetists, reimbursed by Medicare or purchased from commercial sources).

**Population:** Major amputees from Operation Enduring Freedom and Operation Iraqi Freedom.

There is no restrictions on age, gender or ethnic group.

**Progress:** We have mailed 170 surveys and had an approximate 30% response rate. We believe this is due to the fact that potential subjects change addresses multiple times following an amputation. As a result of this, we are in the process of requesting a modification to the protocol that allows us to contact each warrior with an amputation up to 3 times to invite study participation, as this will give us a better chance of finding them.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207026	<b>Status:</b> Completed
<b>Title:</b> Where There's Smoke, is There Disease? A Study of Environmental Airborne Exposures in Soldiers Returning From Iraq		
<b>Principal Investigator:</b> COL Michael J. Sigmon, MC		
<b>Department:</b> Preventive Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Andrew R. Wiesen, MC		
<b>Start - Completion:</b> 12 Dec 2006 - Jun 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to determine the incidence of respiratory illnesses in soldiers from the 3rd Brigade who report environmental airborne exposures while serving in Iraq for a one year tour.

**Technical Approach:** A retrospective cohort study of DD2796 post deployment health assessment questionnaires from the 3000 soldiers from the 3rd Brigade, 2 ID who deployed to Iraq in 2004 and a smaller population of soldiers who deployed to BRIGHT STAR about the same period will be linked to electronic ICD9 codes and responses regarding smoking from the Health Risk Assessment questionnaires from the same soldiers will be linked to study the association between self report of environmental airborne exposures and subsequent respiratory symptoms and medically diagnosed respiratory illness within the first 6 months of returning from Iraq. Outcome variables: include respiratory illness as defined by a specific set of ICD9 codes, (attached). Data analysis will be performed with logistic regression for dichotomous outcome, (disease yes no / exposure yes no). Since there is a crude gradation of exposure the independent variable may be examined further using linear regression.

**Progress:** This protocol was reported as completed in June 2007. This study of a cohort of 2,229 combat arms Soldiers who deployed to Iraq in October 2003 for approximately one year did not find an increased risk of developing respiratory illness within six months of returning from Iraq in Soldiers who reported at least one of ten airborne environmental exposures biologically plausible to cause illness, or a combination of some of these exposures. Recognition of occupational asthma and related respiratory conditions is difficult given the complex nature of occupational dose-response and temporal relationships with respiratory illness, and the complex nature of these illnesses themselves which are often strongly associated with non-occupational exposures. This study provided a novel, economical method to study the association between occupational exposures and respiratory disease based on improving disease surveillance within the Department of Defense. The study could be improved upon by obtaining specific information on occupation and better quantifying exposures and tobacco use. Further epidemiological studies are needed to confirm these findings and to develop surveillance strategies so that the burden of occupational respiratory disease can be reduced in this at risk population.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205099	<b>Status:</b> Completed
<b>Title:</b> CD4+ T Cell Epitope Identification for Protective Antigen of Bacillus Anthracis		
<b>Principal Investigator:</b> LTC Andrew R. Wiesen, MC		
<b>Department:</b> Preventive Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.; CPT Michele A. Soltis, MC; William W. Kwok, Ph.D.		
<b>Start - Completion:</b> 13 Dec 2005 - Mar 2007	<b>Funding:</b> Benaroya Research Institute via CRADA	<b>Periodic Review:</b> 25 Jun 2007

**Study Objective:** To describe CD4+ T cell epitopes of the Protective Antigen of Bacillus.

**Technical Approach:** This is a purely descriptive, basic science study, intended to further understanding of how the human immune system responds to anthrax vaccine. Up to 30 individuals who have received at least 3 doses of anthrax vaccine will be asked to undergo HLA typing (cheek swab). Those with a common HLA type will be asked to give a sample of blood (maximum of 120 cc) for epitope mapping of CD4+ cells. The participants will be drawn from the Fort Lewis active duty and former active duty population. Data analysis will be from flow cytometry methods. As there is no formal hypothesis testing, there will be no formal statistical analysis.

**Progress:** A sufficient number of subjects from all HLA types have been enrolled, and 17 additional blood draws were completed on previously enrolled individuals. Subject enrollment is likely complete, but an additional few subjects may be needed. There were no adverse events during the past year.

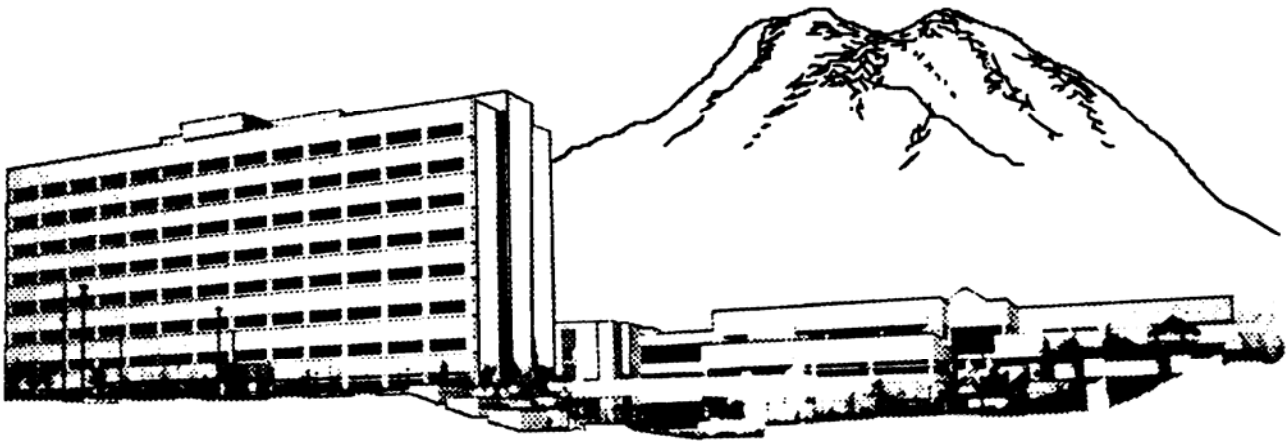
### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207028	<b>Status:</b> Ongoing
<b>Title:</b> An open-label randomized, controlled pilot study of the tolerability, compliance, and short-term effectiveness of rifampin vs. isoniazid for the treatment of latent tuberculosis infection		
<b>Principal Investigator:</b> LTC Andrew R. Wiesen, MC		
<b>Department:</b> Preventive Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Christopher T. Littell, MC; COL James E. Cook, MC		
<b>Start - Completion:</b> 12 Feb 2007 - Jan 2009	<b>Funding:</b> DCI	<b>Periodic Review:</b> 11 Dec 2007

**Study Objective:** Evaluate the tolerability, side-effects, and short-term effectiveness of rifampin versus isoniazid for the treatment of latent tuberculosis infection

**Technical Approach:** Consecutive patients presenting to the Latent Tuberculosis Clinic who meet entry criteria and consent to participate, will be randomized to receive either a 4 month course of rifampin or a 9 month course of isoniazid therapy. Additional blood work will be obtained to monitor for side-effects of the medications. Subjects will be followed for up to 2 years following completion of therapy to assess for progression to active tuberculosis. Major end-points are: compliance, tolerability, and efficacy.

**Progress:** This greater than minimal risk protocol was initially approved by the IRB 12 December 2006, and final approval received 12 February 2007. Enrollment began in April 2007, with approximately one to two subjects enrolled per week. At the time of this report, one subject had completed treatment, and two subjects were dropped from the study secondary to non-compliance with follow-up visits. There have been no significant adverse events.



# **Detail Summary Sheets**

Department of Psychiatry

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204089	<b>Status:</b> Ongoing
<b>Title:</b> A Placebo-Controlled Trial of Prazosin vs. Paroxetine in Combat Stress-Induced Nightmares and Sleep Disturbance		
<b>Principal Investigator:</b> LTC Kris A. Peterson, MC		
<b>Department:</b> Psychiatry	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Larry G. Knauss, Ph.D.; LTC Michael E. Doyle, MC; Christopher Gross M.D.; Elaine R. Peskind, M.D.; Miles M. McFall, Ph.D.; Murray A. Raskind, M.D.; Kirsten Rohde, RN, BSN; Daniel Warren; Bradford L. Felker, MD; Jessica W. Cook, PhD; Daniel J. Conybeare; Bennett Reyes, CRC		
<b>Start - Completion:</b> 29 Oct 2004 - Sep 2008	<b>Funding:</b> VA via MIPR	<b>Periodic Review:</b> 22 May 2007

**Study Objective:** The primary goal of this study is to evaluate the efficacy and tolerability of the alpha-1 adrenergic antagonist prazosin (available commercially since 1972) compared to placebo for combat stress-related nightmares, sleep disturbance and overall function in recently combat-exposed returnees from Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF). A secondary goal is to evaluate the effects of the selective serotonin reuptake inhibitor (SSRI) paroxetine on behavioral symptoms and overall function in this population.

**Technical Approach:** Sample Population/Sample Size includes 90 male and female returning troops from OIF and OEF who manifest persistent combat stress-related nightmares and sleep disturbance. Methods: responses of combat stress-related nightmares, sleep disturbance, and overall stress-related symptom severity will be compared among groups randomized to the alpha-1 adrenergic antagonist prazosin, the SSRI paroxetine, and placebo in a 12-week, double-blind study. Outcome Variables: Clinician-Administered PTSD Scale (CAPS) item 2 "recurrent distressing dreams," item 13 "disturbed sleep," and total CAPS score; Pittsburgh Sleep Quality Inventory; Clinical Global Impression of Change; Hamilton-Depression Rating Scale total scores. Data Analysis Plan: Data will be analyzed for significant differences in outcome variables among treatment groups using generalized estimating equations.

**Progress:** This protocol remains open to subject recruitment and enrollment with thirteen subjects enrolled in this protocol from 5/1/06 and 4/30/07. One subject was a screen failure (hypotension) and twelve subjects were randomized. Of those twelve, three subjects completed (2 paroxetine, 1 placebo); two were removed for compliance issues (1 placebo, 1 blind not broken); one withdrew due to side effects (paroxetine); one withdrew at baseline before drug was taken (blind not broken); one withdrew due to deployment (paroxetine), and one was removed due to worsening depression (prazosin). Three subjects remain actively enrolled.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206011	<b>Status:</b> Ongoing
<b>Title:</b> Prazosin for the Treatment of Trauma Nightmares in PTSD		
<b>Principal Investigator:</b> LTC Kris A. Peterson, MC		
<b>Department:</b> Psychiatry	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Larry G. Knauss, Ph.D.; Elaine R. Peskind, M.D.; Miles M. McFall, Ph.D.; Murray A. Raskind, M.D.; Bradford L. Felker, MD; Jessica W. Cook, PhD; Bennett Reyes, CRC		
<b>Start - Completion:</b> 22 Dec 2005 - Sep 2010	<b>Funding:</b> DCI	<b>Periodic Review:</b> 23 Oct 2007

**Study Objective:** The primary goal of this study is to evaluate the efficacy and tolerability of the alpha-1 adrenergic antagonist prazosin (available commercially since 1972) compared to placebo for combat stress-related nightmares, sleep disturbance and overall function in recently combat-exposed returnees from Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF).

**Technical Approach:** Men and women (120 subjects) with both persistent (> one month duration) troublesome combat stress-related nightmares (CAPS "recurrent distressing dreams" item 5 [maximum score = 8]) and sleep disturbance (CAPS "difficulty falling or staying asleep" item 5 out of a maximum score of 8) who are in good general health and are not taking exclusionary medications are eligible for this study. This is a double-blind, placebo-controlled treatment study of prazosin in combat-exposed persons who have trauma-associated nightmares and sleep disturbance. After a titration period (1-8 weeks in duration) to reach "optimum" dose (up to a maximum of 25 mg/day of prazosin for subjects who weigh less than 250 lbs and 30mg/day of prazosin for subjects who weigh more than 250 lbs), subjects will come to the clinic every two weeks to undergo efficacy evaluation. After the treatment period, the blind will be broken and subjects will be referred to their primary mental health provider for further treatment. Subjects will come in to the clinic for follow-up visits 12 and 26 weeks after the treatment period ends.

Outcome measures will include Clinical Global Impression of Change (CGIC), Recurrent Distressing Dreams and Difficulty Falling and Staying Asleep items of the Clinician-Administered PTSD Scale (CAPS), PTSD Dream Rating Scale (PDRS), Nightmare Frequency Questionnaire (NFQ), Insomnia Severity Index (ISI) and Pittsburgh Sleep Quality Index (PSQI). Depression and quality of life will also be assessed with the Hamilton Depression Rating Scale (HAM-D) and Quality of Life Index (QOLI). The primary intent-to-treat (ITT) efficacy assessment will compare the prazosin and placebo group's CGIC scores at 8 weeks. Since response is not anticipated to be progressive, any missing observations will be imputed using the last observation carried forward (LOCF) procedure. The CAPS Recurrent Distressing Dreams and Difficulty Falling or Staying Asleep items, total CAPS, Mississippi Scale, PSQI, ISI, PDRS, NFQ, Ham-D, and QOLI item will be analyzed as a continuous response measure. Rates of change in response measures will be evaluated according to ITT between the prazosin and placebo groups using an analysis of covariance model with the 8-week values as the response measure and baseline measure as a covariate along with any potential confounding variables. The median time to study discontinuation (in those patients who drop out secondary to unacceptable adverse effects) will be compared between the two treatment groups using the Cox proportional hazards model. Frequency of individual adverse event occurrence will be compared by chi square and adverse event severity by unpaired t-test between prazosin and placebo conditions to estimate the clinical significance of potential prazosin adverse effects.

**Progress:** As of September 2007, 17 subjects consented into this study at MAMC. Four subjects failed screening and thirteen subjects were randomized. Of these, six are actively participating in the blind portion of the study, two are actively participating in the open label, follow-up portion of



the study, three have been lost to follow-up (at visits T6, T8 and Wk 01), and one withdrew consent at T3 due to non-descript ill feeling. This subject would not provide any additional information. One subject was terminated from the study at baseline and enrolled in a more appropriate study. Subject recruitment continues.

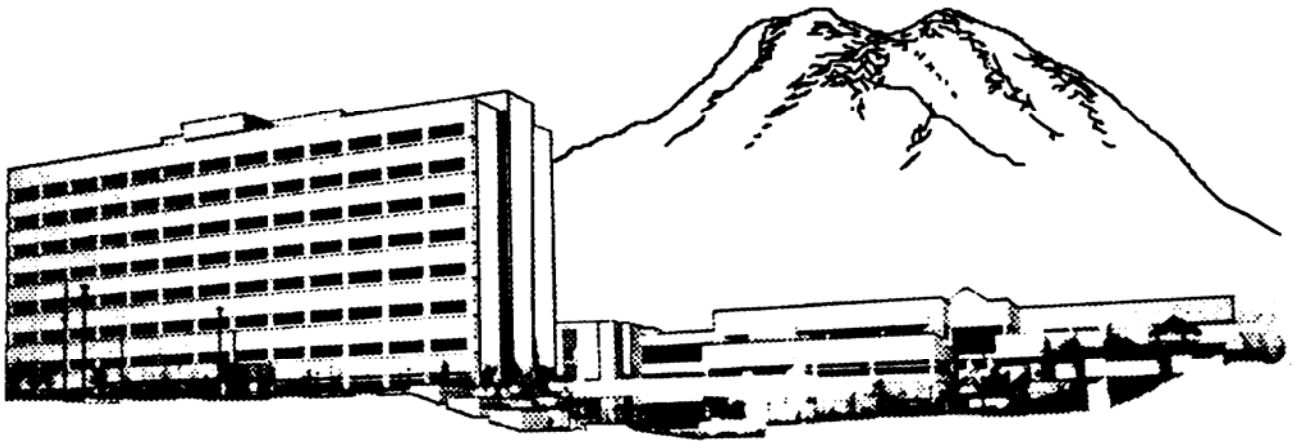
### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207020	<b>Status:</b> Ongoing
<b>Title:</b> The Impact of Parental Wartime Deployment on Adjustment of Children		
<b>Principal Investigator:</b> LTC Kris A. Peterson, MC		
<b>Department:</b> Psychiatry	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Larry G. Knauss, Ph.D.; Patricia Lester, MD; MAJ Katie C Gabriel, MC; Robert Pynoos, MD; Naihua Duan, PhD; William Saltzman, PhD		
<b>Start - Completion:</b> 13 Feb 2007 - Dec 2007	<b>Funding:</b> UCLA via DCI	<b>Periodic Review:</b> 23 Oct 2007

**Study Objective:** The objective of this study is to assess the behavioral and emotional impact of parental wartime deployment on children age 6-12.

**Technical Approach:** This study proposes to examine prevalence of social, behavioral, and emotional problems for children affected by a parent's wartime deployment and examine potential background and mediating factors of child adjustment. Recruited families (n=150) with a 6-12 year child (n=180) will be stratified into 3 strata: a) 50 families with children in which an active duty parent is currently deployed in Iraq; b) 50 families with children in which a active duty parent returned from Iraq to Fort Lewis within the last six months; and c) 50 families with children in which the active duty parent has never deployed in Iraq. This descriptive study will clarify correlates of adaptive and maladaptive adjustment in children exposed to a parent's wartime deployment, as well as post deployment reunion with a parent, providing information about potential protective and risk factors for adjustment in these children. These findings will be used to develop appropriate prevention/intervention programs that strengthen military families during wartime deployment.

**Progress:** This minimal risk protocol was initially approved by the IRB 21 November 2006, and final approval received 13 February 2007. Protocol documentation was released to the study staff following CRADA/SOW approval 24 April 2007. A consent form revision and the addition of an associate investigator were submitted and approved.



# **Detail Summary Sheets**

Department of Psychology

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206062	<b>Status:</b> Completed
<b>Title:</b> Military Readiness Risks: Leader Perspectives Impact on Mandatory Addiction Referrals		
<b>Principal Investigator:</b> Jolee N. Darnell, MSW, LICSW, CDP		
<b>Department:</b> Psychology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Lori A. Loan, RNC, PhD; Brenda M. Wilson, MS, LPA, CDP; Ross A. Echterling, BS, CDP; Joseph D. Darnell, BA		
<b>Start - Completion:</b> 28 Feb 2006 - Mar 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The goal of the research is to determine whether there are other interventions or education that could be used to target and improve the referral rates and ultimately military readiness.

**Technical Approach:** This proposal uses a qualitative research method approach to examine questions related to the impact of leader attitudes and operational tempos on completion of mandatory substance abuse referrals. Action research methods will be used, including ex post facto review of existing data and interviews and focus groups with key stakeholders (Active Duty Fort Lewis military leaders at the levels of platoon, company, battalion, and brigade). The researcher will coordinate with the First Corps Surgeon's office and each Brigade Surgeon's office to recruit focus group and individual interview volunteers from each Brigade size unit at the installation. Recruitment requests will be made through the process of Officer Professional Development (OPD) and Non-Commissioned Officer Professional Development (NCOPD) during required training on health and health care related topics.

Following documented informed consent, the study will use interviews and focus group discussions to generate information for the research questions. Discussion topics will include: participant understanding of regulatory referral requirements, participant philosophy about alcohol and drug use in the military; participant understanding of substance abuse and dependence; perspectives about positive and negative aspects of the Army's mandatory substance abuse referral program; participant perspectives on data trends; participant perspectives about relationships between military mission requirements and mandatory substance abuse referral processes. Before focus groups and interviews are conducted, specific dialogue will be validated for appropriateness by an expert panel of line leaders and professionals involved in the referral process. The goal is to get the experts to provide guidance and critique of the specific discussion topics to be used in the focus groups and interviews.

**Progress:** This protocol was reported completed in February 2007. Results: Military leaders generally view the substance abuse referral process as a meaningful tool for preserving military readiness. Many of the leaders interviewed expressed concern about the data reports reflecting the percentage of Soldiers who apparently did not get referred after an identified substance abuse incident. Most of the leaders agreed that operations tempos and multiple competing demands did have an impact on completing referrals, even when they believed it was the right thing to do. Most of the leaders indicated that policy or regulatory requirements carried less influence than their beliefs about personal and professional values and responsibilities, and the stated or implied focus of their change of command. Data reflected in the interview responses indicate that military leaders use input from military ethical decision making models in their routine practice for decision making specific to choices related to mandatory substance abuse referrals. Findings of the interviews reflected a need for the substance abuse program to tailor substance abuse educational programs to include opportunities for discussion about the ethical dilemmas inherent in meeting

the required standards for mandatory substance abuse referral in a high operations tempo environment.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207011	<b>Status:</b> Ongoing
<b>Title:</b> Corresponding Authors' Compliance with E-mail Requests for Additional Information		
<b>Principal Investigator:</b> COL Gregory A. Gahm, MS		
<b>Department:</b> Psychology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Mark A. Reger, PhD; CPT Greg M. Reger, MS; Barbara A. Lucenko, PhD		
<b>Start - Completion:</b> 27 Oct 2006 - Oct 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 4 Oct 2007

**Study Objective:** The objective of this study is to determine the rate of compliance with e-mailed requests for additional data to the corresponding authors of peer reviewed professional journal articles.

**Technical Approach:** The Tables of Contents of relevant journals will be examined for the number of qualifying articles (empirical regular articles or brief reports). A random number generator will select 200 articles per year from medical journals and 200 per year from the psychological journals. For each year, half of the corresponding authors will receive a Standardized General Interest request and half will receive a Standardized Meta-Analysis request. An additional 200 corresponding authors will be selected to receive a Specific Data Request (a request specific to data mentioned in their article).

**Progress:** The 2000 standardized email requests have been sent as described per protocol. The 200 specific requests for data have not been sent, but investigators do not plan on completing that phase of the study due to the resources it would require. Investigators are currently in the process of coding the email responses received during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207073	<b>Status:</b> Ongoing
<b>Title:</b> Evaluation of the Post Deployment Health Assessment (PDHA) & Post-Deployment Health Reassessment (PDHRA) Program		
<b>Principal Investigator:</b> COL Gregory A. Gahm, MS		
<b>Department:</b> Psychology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Mark A. Reger, PhD; Robert D. Swanson, PhD; Ron C. Kessler; Tammy L. Williams, RN, CCRC; CPT Christopher A. Myers, MC; Matthew C. Mishkind, PhD; Jaime A. Wilson, PhD; Hongtu Chen, PhD; Laura E. Boye, MA; LTC Telita D. Crosland, MC		
<b>Start - Completion:</b> 9 Mar 2007 - Sep 2007	<b>Funding:</b> DoD via MIPR	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objectives of this study are to (1) assess how well the PDHA, PDHRA, and SWAPP processes detect a deployment-related mental health concern requiring referral for treatment compared to the referral rate based on a gold standard evaluation by a psychologist using the Structured Clinical Interview for DSM-IV (SCID) diagnostic algorithm, (2) examine whether endorsing the self-report questions on mental health contained on the DD 2796, DD 2900, or HRA-II correlate to diagnoses of depression, anxiety, PTSD, or alcohol abuse as determined through the SCID evaluation by a psychologist, (3) assess how well the PDHA, PDHRA, and SWAPP processes detect a deployment-related physical health concern requiring referral for treatment compared to the referral rate based on a physical exam by a clinician, (4) examine whether there is a positive correlation between being referred for a mental or physical health concern and functional limitations as measured by the SF-36, (5) examine whether endorsing the self-report questions on physical health on DD Forms DD2796, DD2900, or HRA-II correlate to functional limitations as measured by the SF-36, and whether different conditions relate to greater or lesser impairment, (6) examine health care utilization data post-assessment to determine whether service members participating in the validation groups were ultimately diagnosed with any physical or mental health condition, and relate those diagnoses to the results of the PDHA, PDHRA, or SWAPP process, and (7) ascertain Soldier satisfaction with the PDHA, PDHRA, and SWAPP processes and ascertain level of stigma around mental health issues to help guide future post-deployment assessment outreach and implementation planning.

**Technical Approach:** This study has been requested by Congress under Public Law No. 109-163 (H.R. 1815), Section. 731. The study relates to pre-deployment and post-deployment medical exams of certain members of the armed forces. The Secretary of Defense shall conduct a study of the effectiveness of self-administered surveys included in pre-deployment and post-deployment medical exams, including the mental health portion of the surveys, of members of the Armed Forces that are carried out as part of the medical tracking system required under section 1074f of title 10, United States Code.

The Post-Deployment Health Assessment (PDHA) and the Post-Deployment Health Reassessment (PDHRA) are currently in use by all branches and components of the military to assess the health status of service members returning from combat theaters (re-deployment). Deployment-related health symptoms sometimes do not emerge until several months or longer after return from theater. Thus, these two assessments-one just following re-deployment (PDHA) and the second three months out from re-deployment (PDHRA)-are used to gather information essential to the core mission of force health protection.

The initial work on the validation of the post-deployment processes will take place at Fort Lewis in Washington State. At Ft. Lewis, there is a unique opportunity to confirm (i.e., validate) that three post-deployment processes are working as expected. At Ft. Lewis, the PDHA process and an enhanced version of the PDHRA process, called SWAPP, are used to assess Soldiers post-

deployment. With some relatively minor adjustments to the SWAPP process, we will also validate the more standard PDHRA process at Ft. Lewis.

**Progress:** This minimal risk protocol received initial approval by the Expedited Review Committee on 9 March 2007. During FY07, subjects were enrolled and data collected from Fort Wainwright, Alaska. Enrollment and data collection continues at Fort Lewis. Amendments have been submitted to add additional investigators to assist with data collection.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205019	<b>Status:</b> Ongoing
<b>Title:</b> Theory-Guided Anticipatory Guidance		
<b>Principal Investigator:</b> Patti L. Johnson, Ph.D.		
<b>Department:</b> Psychology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Christine Moon, PhD		
<b>Start - Completion:</b> 3 Dec 2004 - Oct 2005	<b>Funding:</b> UW/PLU	<b>Periodic Review:</b> 13 Nov 2007

**Study Objective:** The objective is to test the application of the prevailing psychological theory of persuasion on information delivery to mothers of young infants.

**Technical Approach:** This study will test the use of the Elaboration Likelihood Model (ELM) of persuasion on attitude change of 200 mothers of newborn infants regarding early shared reading with their infants. The two independent variables are 1) two levels of participants' live birth (para) status and 2) two formats of a brief education intervention. The education intervention will be administered during the last 10 minutes of a 20-minute session to be scheduled after the daily Mother/Baby Unit discharge class. During the first 10 minutes, informed consent will be obtained and three brief questionnaires will be completed: a personal information questionnaire, the Sensations during Pregnancy and Life Events Questionnaire, and a questionnaire on attitudes about early shared reading. The effect of intervention will be assessed two months later by re-administering the questionnaire on attitudes about early shared reading. Para status is a marker for level of distraction from parenting the new baby, important for ELM application. Verification of level of distraction will be made by using the Sensations during Pregnancy and Life Events Questionnaire.

At the conclusion of data collection, there will be 40 mothers in each of the 4 intervention groups (2 para statuses X 2 formats.) A control group (n=40) will receive general information on speech/language development. The dependent variable will be difference scores on the pre- and post-intervention questionnaires on attitude about early shared reading, and the difference scores will be analyzed using analysis of variance. It is predicted that there will be a statistically significant interaction effect between para status and intervention format. Further, difference scores of both intervention groups will be higher than control group scores. Results of the experiment are expected to inform the practice of information delivery to patients, specifically in anticipatory guidance in pediatrics.

**Progress:** At the time of this report, 219 participants enrolled, which represents 73% of the 300 planned for this study. Subject enrollment continues.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206118	<b>Status:</b> Ongoing
<b>Title:</b> User Centered Design Feedback for the Virtual Iraq		
<b>Principal Investigator:</b> CPT Greg M. Reger, MS		
<b>Department:</b> Psychology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Gregory A. Gahm, MS; Mark A. Reger, PhD; John L. Miller, MD; Barbara A. Lucenko, PhD; Albert A Rizzo, PhD; CPT Roberta L. Shepard, MC; Robert D. Swanson, PhD; Susan J. Duma, MS; ; CPT Mark J. Baird, MS		
<b>Start - Completion:</b> 19 Oct 2006 - Jul 2007	<b>Funding:</b> TATRC	<b>Periodic Review:</b> 28 Aug 2007

**Study Objective:** To obtain user-centered design feedback from healthy, non-patient soldiers to guide the project development of a virtual reality application (VR Iraq) intended for future use to treat a wide range of possible traumatic combat experiences.

**Technical Approach:** Following consent, Soldiers will complete a brief demographic questionnaire and PTSD Checklist, which is a validated PTSD screening tool. The consenting investigator will review these documents and ensure that the participant meets inclusion/exclusion criteria. In the case that the participant self-reports significant levels of trauma related symptomatology, the investigator will discontinue formal participation in the project and will offer to discuss their responses on the survey and escort participants to a private location to talk (e.g., Behavioral Health Clinic or Soldier Readiness Service) to discuss options for referral and treatment, if indicated. Participants who meet inclusion/exclusion criteria will utilize the two VR scenarios. The current city scenario has the appearance of a desolate set of low populated streets comprising old buildings, ramshackle apartments, warehouses, a mosque, factories, and junkyards. The second scenario is a convoy scenario in which the user navigates down paved and dirt desert roadways with occasional areas of vegetation, battle wreckage, and debris. As soldiers navigate through these environments, the investigator will activate currently available trigger stimuli. Currently, the VR Iraq allows the controller to introduce audio triggers (i.e., incoming mortars, weapons fire, voices, wind, etc.) and audiovisual triggers (e.g., helicopter flyovers). Total time utilizing the VR Iraq will be approximately 5 minutes.

**Progress:** Since initiation of enrollment in October 2006, data has been collected from 67 Soldiers on location with the 47th CSH and preliminary analyses conducted. Several participants consented to participate in the project, but were excluded when they did not meet full inclusion criteria.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206077	<b>Status:</b> Ongoing
<b>Title:</b> Army Suicide Event Report: Data Analysis		
<b>Principal Investigator:</b> Mark A. Reger, PhD		
<b>Department:</b> Psychology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Gregory A. Gahm, MS; Barbara A. Lucenko, PhD		
<b>Start - Completion:</b> 10 Apr 2006 - Mar 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 13 Mar 2007

**Study Objective:** To establish an effective and efficient model of risk assessment for suicide, suicide ideation, and suicide attempts using existing data from the Army Suicide Event Report (ASER).

**Technical Approach:** This study is a retrospective review and exploratory analysis of Soldiers for whom ASER data exists. Initial review reveals 742 records as of November 2005. The study will track suicide behavior for 2005-2007, using exploratory analyses to detect trends and risk and protective factors.

**Progress:** A total of 1,071 ASERs have been submitted since initial protocol approval was received on 10 April 2006. Analyses have not yet been conducted for this protocol to date. Note: The number of submitted ASERs reported in the last progress report indicated 1128 for FY06. It was a mistake to report FY06 data, as the protocol was not approved until April 10, 2006. ASERs submitted prior to the approval date are not considered a part of this study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206088	<b>Status:</b> Ongoing
<b>Title:</b> Exposure to Death and Dying and Mental Health Response in Operation Iraqi Freedom		
<b>Principal Investigator:</b> Mark A. Reger, PhD		
<b>Department:</b> Psychology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Shira Maguen, PhD; COL Gregory A. Gahm, MS; Barbara A. Lucenko, PhD		
<b>Start - Completion:</b> 8 May 2006 - May 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 7 May 2007

**Study Objective:** To test a model demonstrating the relationship between exposure to death and dying, mental health outcome, and functional impact following deployment to Iraq.

**Technical Approach:** The Health Risk Appraisal II (HRA-II) is administered 90 days post-deployment. Soldiers completed an automated version of the HRA-II in groups scheduled according to specific Active Duty units. Groups were reportedly scheduled according to unit re-deployment status. The screening may have occurred at any point between 60 and 120 days after returning from deployment, although the typical timeframe has been reported as between 60-90 days. A data transfer process serves to populate a secure Oracle database housed within the Army Behavioral Health Technology Office. Algorithms written into software score the clinical scales and generate reports for Behavioral Health (BH) routing and provider use. All soldiers are then seen by a BH provider on site and follow up clinical referrals are made based on both screening and interviews. Prior to analyses for this project, appropriate fields from the database will be copied stripped of all identifying information (name, social security number, and contact information). The relevant variables outlined in this proposal will be sent to the San Francisco VA Medical Center for the specified data analysis. Dr. Maguen will not have access to any of the identifying information (names and social security numbers, and contact information) at any point during the study. Also, the data will continue to be owned by MAMC.

**Progress:** The Health Risk Appraisal II (HRA-II) for 12,315 subjects was available for retrospective review. No analyses have been conducted to date and the protocol remains ongoing.

### Detail Summary Sheet

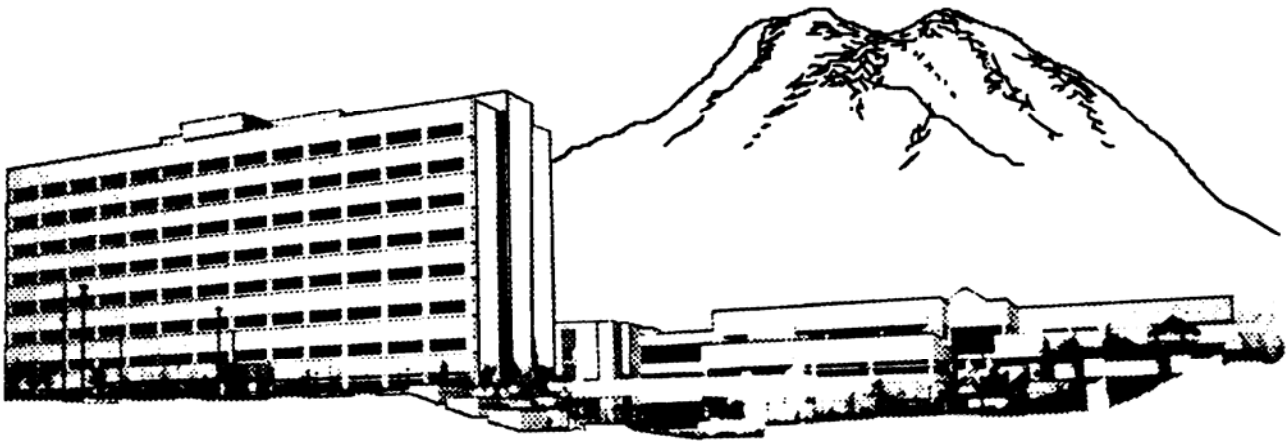
<b>Date:</b> 30 Sep 07	<b>Number:</b> 207114	<b>Status:</b> Ongoing
<b>Title:</b> Identifying Image Management in Neuropsychological Testing with the CVLT-2, and the Malingering Index and Rogers' Discriminant Function of the PAI in Military Organizations		
<b>Principal Investigator:</b> John R Steigerwald, DAC		
<b>Department:</b> Psychology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 6 Aug 2007 - Jul 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective of this study is to examine the ability of components of the California Verbal Learning Test-2 and the Personality Assessment Inventory to distinguish between legitimate and exaggerated performance in actual patients with presentations of neuropsychological problems.

**Technical Approach:** This study is an investigational, correlation study that uses Neuropsychology Clinic archival data from April 2002 through September 2006, approximately 350 protocols. The study protocols used will be those of active duty service members from 18 through 55 years old, referred for neuropsychological evaluation for MEB, PEB and fitness for duty questions. The variables to be assessed include: the Recognition Memory subtest score and the Forced Choice score from the CVLT-2; the Malingering Index score, Rogers Discriminant Function, Negative Image Management and Positive Image Management of the PAI; the impairment scores of the Neuropsychological Deficit Scale and the Halstead-Reitan Impairment index; and the final neuropsychological diagnosis.

The neuropsychological diagnoses will be separated into four categories: Cognitive Disorder with supporting positive laboratory and /or radiographic imaging; Cognitive Disorder without supporting positive laboratory and /or radiographic imaging; No cognitive disorder; Malingering supported by observation, egregious results on malingering tests, and reports from external sources. The results of the testing will be analyzed by both linear regression, and multiple regression statistical processes in a SPSS 11.0 program. The study will attempt to demonstrate that patients with diagnoses of cognitive disorder with positive scanning results will produce no significant test results on the malingering tests or scales. Also, the study will attempt to demonstrate that patients diagnosed with malingering will not produce significant results on neuropsychological tests. If these statements are true, the third demonstration would involve attempting to identify the tests or combination of tests that would predict both cognitive and image management.

**Progress:** This minimal risk protocol received final approval by the Expedited Review Committee, effective 6 August 2007.



# **Detail Summary Sheets**

Department of Radiology

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 202117	<b>Status:</b> Ongoing
<b>Title:</b> Intravenous Administration of 131 I-6-B Iodomethylnorcholesterol (NP-59) for Adrenal Evaluation and Imaging		
<b>Principal Investigator:</b> LTC Antonio G. Balingit, MC		
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL (Ret) Jerome L. Billingsley, MD; Jane E. Besich-Carter, BS, BCNP; CPT Deborah E. Floyd, MS		
<b>Start - Completion:</b> 7 Jan 2004 - Jul 2003	<b>Funding:</b> DCI	<b>Periodic Review:</b> 21 Aug 2007

**Study Objective:** Clinical evaluation of NP-59 as a diagnostic agent for the detection of adrenocortical disorders.

**Technical Approach:** The drug to be used in this study, NP-59, is investigational and will be used under IND number 12605, which is held by the University of Michigan. This study will be performed in humans of either sex only after complete evaluation by the Endocrinology Service of MAMC. All female patients between the ages of twelve and fifty-five will have a serum B-HCG determination except those who had a hysterectomy. Pregnant or lactating patients will be excluded. This agent will be administered to children less than 18 years of age only for exceptional reasons with the approval of the Chief, Nuclear Medicine Service and Chief, Pediatric Endocrinology Service and only after other alternative procedures are determined to be inappropriate. Ideally, studies in women of childbearing capability are performed during the first 10 days post-menses. NP-59 will be obtained in pharmaceutical form from the University of Michigan Nuclear Pharmacy. In house quality control, including determination of radionuclidic and radiochemical purity, will be performed on all shipments of NP-59 prior to human use. NP-59 will be administered by slow intravenous injection with a dose of 2mCi in adults, 15 UCi/kg in children except where the benefit to risk ratio warrants a higher dose. Under no circumstances will more than 2.2 mCi be administered. Lugol's solution, 5 drops twice daily starting one day before injection and continuing for two weeks, will be used to block thyroid uptake of radionuclide. Planar and SPECT images will be obtained on the 3rd, 4th and 5th days after injection using a dual detector scintillation camera connected to an on-line computer. Studies will be performed in accordance with the protocol "<sup>131</sup>I-6-B iodomethylnorcholesterol." Informed consent will be obtained prior to entry into the study.

**Progress:** This expanded access protocol remains ongoing with no patients requiring enrollment during FY07. The radiopharmaceutical is an infrequently utilized 'orphan' drug, has not been FDA approved, and can only be procured as an IND. Nuclear Medicine Service maintains this protocol in order to utilize the drug if a need arises.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204069	<b>Status:</b> Ongoing
<b>Title:</b> SWOG RTOG 0212, A Phase II/III Randomized Trial of Two Doses (Phase III-Standard vs. High) and Two High Dose Schedules (Phase II-Once vs Twice Daily) for Delivering Prophylactic Cranial Irradiation for Patients With Limited Disease Small Cell Lung Cancer		
<b>Principal Investigator:</b> COL John B. Halligan, MC		
<b>Department:</b> Radiology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC William B. Reece, MC		
<b>Start - Completion:</b> 20 Jul 2004 - May 2007	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 16 Apr 2007

**Study Objective:** (1) To determine the impact of an increase in the total PCI dose on the incidence of brain metastases at a minimum of 2 years of patient follow up; two PCI dose levels will be compared: 25 Gy (standard dose PCI) versus 36 Gy (high dose PCI) in limited disease small cell lung cancer (LD SCLC) patients in complete remission, whatever the initial treatment. (2) To determine the impact of PCXI dose of overall and disease-free survival; (3) To determine the impact of PCI dose on quality of life and late treatment sequel, 4) To determine the impact of PIC dose and schedule on the incidence of chronic neurotoxicity, and (5) To determine the impact of PCI dose and schedule on quality of life.

**Technical Approach:** About five to seven subjects per year would potentially eligible for this protocol at Madigan Army Medical Center. The protocol randomizes subjects to receive one of three doses of prophylactic cranial irradiation. Arm I subjects receive 2.5 G ray once daily for 10 fractions for a total of 25 G ray. Arm II subjects receive 2.0 G ray once daily for 18 fractions for a total of 36 G ray. Arm III subjects receive 1.5 Gray once daily for 24 fractions for a total of 36 G ray. The study will examine the incidence of brain metastases as the primary end point and assess the cognitive and neurologic side effects of subjects on the above treatment doses and delivery schedules through neurotoxicity/neuropsychological testing. The results of this study may modify the standard dose schedule currently used in the delivery of this critical treatment.

**Progress:** This protocol closed enrollment during FY06, with one subject enrolled who continues to be followed. A change in the role of principal investigator from LTC Reece to COL Halligan was submitted and approved. No adverse events have been reported.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207051	<b>Status:</b> Ongoing
<b>Title:</b> CTSU RTOG 0521, A Phase III Protocol of Androgen Suppression (AS) and 3DCRT/IMRT vs. AS and 3DCRT/IMRT Followed by Chemotherapy with Docetaxel and Prednisone for Localized, High-Risk Prostate Cancer		
<b>Principal Investigator:</b> COL John B. Halligan, MC		
<b>Department:</b> Radiology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Joseph P. Brooks, MC; LTC David E. McCune, MC; MAJ Angela G. Mysliwicz, MC; MAJ Jasmine T. Daniels, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 5 Mar 2007 - Feb 2012	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 2 Jan 2008

**Study Objective:** The primary objective of this study is to assess the relative efficacy of the combination of androgen suppression (AS) + radiotherapy (RT) followed by androgen suppression vs. AS + RT followed by docetaxel and prednisone chemotherapy + androgen suppression in a population of patients with clinically localized prostate cancer with unfavorable prognostic factors. The primary endpoint will be overall survival.

Secondary objectives are to assess the differences between the two treatment arms for: biochemical control (freedom from PSA failure), local control, freedom from distant metastases, disease-free survival, and incidence of adverse events. In addition, the following will be assessed: validity of PSA-defined endpoints as a surrogate for the primary objective and the time interval between biochemical failure and distant metastases with respect to testosterone level.

**Technical Approach:** This multi-institutional phase III trial sponsored by the Radiation Therapy Oncology Group (RTOG) will evaluate the addition of Docetaxel/Prednisone chemotherapy to radiation therapy plus 2 years of androgen suppression for high risk prostate cancer. All patients will be treated with current standard of care 3D conformal or intensity modulated radiation therapy to 72-75.7Gray external beam radiation plus 2 years of LHRH agonist. Patients will be randomized to plus or minus Docetaxel/Prednisone for 6 cycles starting 28 days after completion of radiation to be given concurrently with ongoing LHRH therapy.

**Progress:** This greater than minimal risk protocol received initial approval by the IRB 23 January 2007, and final approval on 5 March 2007. Amendment #3 updates to the information about risks, and tissue and specimen questions was submitted and approved. No subjects enrolled during FY07.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207111	<b>Status:</b> Ongoing
<b>Title:</b> Reduced PTV Margins for the Treatment of Prostate Cancer with IMRT Using Real-Time, State-of-the-Art Motion Tracking with the Calypso 4D Localization System®: A Feasibility Study		
<b>Principal Investigator:</b> COL John B. Halligan, MC		
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Joseph P. Brooks, MC; LTC Karen C. Baker, MC		
<b>Start - Completion:</b> 27 Sep 2007 - Nov 2009	<b>Funding:</b> Battelle	<b>Periodic Review:</b> N/A

**Study Objective:** This study will look at the feasibility of treating a smaller volume in the definitive radiation therapy of prostate cancer using a unique organ tracking system. The protocol objective is to determine if targeted radiation therapy with reduced treatment margins can be adopted as feasible for routine clinical use. This will be assessed by the set up time, treatment time, total time and number of treatment interventions (repositioning/pausing) caused by organ/target motion beyond planning target volume (PTV) margin using real time localization. Confirmation of feasibility will provide the platform for future advances.

Secondary objective is to analyze dosimetric characteristics of treatment planning using standard methods versus reduced planning target volume expansion (a) Dose Volume Histogram (DVH), bladder and rectum, and (b) Volume receiving 75.6Gy by the prescription dose (V75.6Gy), V70Gy, and V50Gy of bladder and rectum, and to assess the incidence of acute bladder and rectal toxicity based to the RTOG/NCI CTC.

**Technical Approach:** This prospective study at MAMC and VAPS evaluates the clinical utility of a novel real-time localization system allowing smaller volumes of normal tissue to be included in radiation fields and determines dosimetric parameters and adverse effect profiles of radiation therapy using this technology. The sample population will include patients referred to the radiation oncology services of both facilities for definitive treatment of prostate cancer. The study will enroll 40 subjects and evaluate data on 1680 radiation therapy fractions.

Subjects will have Beacon Transponders® implanted into the prostate to more precisely localize the position of the organ during radiation therapy. They will then undergo radiation therapy planning with both standard planning target margins and reduced planning target margins. The patients will be treated with the reduced planning target margin plans using the Calypso 4D Localization System® to monitor, in real time, the position of the prostate target and adjust radiation treatments as required to ensure accurate treatment of the prostate gland with minimal margin. The study will then follow the ability of the treating teams to treat the subjects in a standard radiation therapy time slot and number of treatment interruptions caused by using reduced margins.

The standard and reduced margin plans will be compared with single sided t-tests for key dosimetric parameters of normal tissue exposure. This includes the volume of tissue receiving 75.6Gy (V75.6Gy), V70Gy, V50Gy of both the bladder and rectum as well as dose volume histograms of bladder and rectum. In addition, the incidence of adverse effects on bladder, rectal, and sexual function will be followed weekly during the course of radiation therapy and for one year following completion of treatment.

**Progress:** This greater than minimal risk protocol received initial IRB approval on 24 July 2007, and final approval was received 27 September 2007. The PI reports that enrollment has not yet been initiated.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205024	<b>Status:</b> Ongoing
<b>Title:</b> Computed Tomography of the Abdomen Following Appendectomy		
<b>Principal Investigator:</b> CPT William T. Lewis, MC		
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Andrew E. Fong, MC; CPT Brian C. Beldowicz, MC; MAJ Joseph A. Ronsivalle, MC; LTC John D. Statler, MC		
<b>Start - Completion:</b> 16 Feb 2005 - Feb 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 11 Dec 2007

**Study Objective:** To determine the computed tomography (CT) findings of patients who have recently undergone appendectomy.

**Technical Approach:** Fifty male and fifty female subjects will be recruited while in-hospital following their appendectomy. Relevant labs (serum creatinine) and history (contrast allergy) will be reviewed, and the subjects will be excluded from the study as indicated. Subjects meeting inclusion criteria and wishing to participate in the study will be assigned a random patient number. The PI will secure the code list. The subject will be given an appointment for CT scan of the abdomen on the same day as his follow-up appointment in the surgery clinic. Subjects will arrive at the Dept of Radiology, Computed Tomography section before their surgery clinic appointment. CT technologists will verify the subject's eligibility to undergo the exam. The subject will ingest approximately 1 1/2 liters of oral contrast. An intravenous line will be started. Following adequate time (approximately 2 1/2 hrs) to opacify the small bowel, CT of the abdomen and pelvis with oral and intravenous contrast will be obtained. The i.v. will be removed, and the subject will be discharged to the surgical clinic. Total participation time should take approximately 3 hours.

**Progress:** This protocol remain open to enrollment with 40 subjects enrolled, 10 during the last approval period. Although many patients fit the inclusion criteria, the majority have not been interested in participating. Of the many patients offered the study, only 5 within the last 6 months have agreed. The PI hopes to complete enrollment of the last 10 subjects required to begin data analysis.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207059	<b>Status:</b> Completed
<b>Title:</b> Retrospective Evaluation of Endovascular Interventions for War Related Extremity Injuries at Madigan Army Medical Center		
<b>Principal Investigator:</b> CPT Michael H. Park, MC		
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC John D. Statler, MC; MAJ Andrew S. Bostaph, MC; LTC Benjamin W. Starnes, MC; COL (Ret) Charles A. Andersen, MD		
<b>Start - Completion:</b> 12 Feb 2007 - Feb 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objectives of this study are to (1) describe the scope of service offered at Madigan Army Medical Center for war related vascular injuries to the extremities, as well as documenting the other procedures performed at more forward facilities, (2) document demographic information about the types of patient receiving endovascular interventions, and (3) document other associated procedures performed both in the field and at other medical facilities.

**Technical Approach:** Retrospective chart review of patients treated with endovascular procedures for combat related extremity injuries at Madigan Army Medical Center in 2006. This protocol is a descriptive study only and will not involve statistical analysis or intervention. The purpose of the study is to review the scope of services offered at Madigan in treating these injuries. Data collected will include demographics, as well as detailed information about the injury sustained and the treatment received prior to arriving at Madigan Army Medical Center. Data about the patient's present condition will also be obtained, as available. Given the prevalence of these injuries in Wartime, information about various treatment modalities is extremely important.

**Progress:** This minimal risk protocol received initial approval by the Expedited Review Committee on 12 February 2007. No changes to the protocol or progress reports have been submitted.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206053	<b>Status:</b> Terminated
<b>Title:</b> NSABP B-39 / RTOG 0413 A Randomized Phase III Study of Conventional Whole Breast Irradiation (WBI) Versus Partial Breast Irradiation (PBI) for Women with Stage 0, I or II Breast Cancer		
<b>Principal Investigator:</b> LTC William B. Reece, MC		
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL John B. Halligan, MC; MAJ Joseph P. Brooks, MC; MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC		
<b>Start - Completion:</b> 5 Jun 2006 - Feb 2011	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 30 Jan 2007

**Study Objective:** Primary objective is to determine whether partial breast irradiation (PBI) limited to the region of the tumor bed following lumpectomy provides equivalent local tumor control in the breast compared to conventional whole breast irradiation (WBI) in the local management of early stage breast cancer.

Secondary objectives are (1) to compare overall survival, recurrence-free survival, and distant disease-free survival between women receiving PBI and WBI, (2) to determine whether PBI delivered on 5 treatment days over a period of 5 to 10 days can provide a comparable cosmetic results to WBI, (3) to determine if PBI produces less fatigue and treatment-related symptoms compared to WBI, (4) to determine if perceived convenience of care is greater for women receiving PBI compared to women receiving WBI and (5) to compare acute and late toxicities between the radiation therapy regimens.

**Technical Approach:** This Phase III, randomized trial will enroll patients with stage 0 (DCIS) or stage I or II invasive adenocarcinoma of the breast with no evidence of metastatic disease who have undergone lumpectomy with cancer-free margins, and have no more than 3 positive axillary nodes. Patients will be stratified according to disease stage, menopausal status, hormone receptor status, and intention to receive chemotherapy. Following stratification, patients will be randomized to receive WBI or PBI. WBI for this study will be standard techniques delivered over 5 to 7 weeks. PBI will utilize the technologies of high dose-rate multi-catheter brachytherapy, high dose-rate single catheter balloon brachytherapy (MammoSite), and three-dimensional conformal external beam radiation therapy. Patients randomized to receive WBI will receive chemotherapy, if applicable, before their radiation therapy. Patients randomized to PBI will receive radiation therapy before chemotherapy, if applicable. For patients who agree to blood and tissue studies, blood will be submitted after randomization but before therapy begins and tissue blocks will be submitted within 3 months after randomization. Patients will have follow-up visits at end of radiation therapy, 4 weeks, 6 months, 12 months, every 6 months through Year 5, then annually through Year 10. The first 482 patients who are having chemotherapy and the first 482 patients who do not intend to receive chemotherapy will have the option of being included in a QOL and cosmesis study. These patients will have 7 QOL questionnaires to complete during the course of treatment and follow-up, and will have three sets of digital photographs taken of their breasts at baseline, Year 1 and Year 3. RTOG will provide a web-based image management system for sites to upload images as JPEG files. Each site will have restricted access to only their image archive, and once images are uploaded they will only be accessible to NSABP reviewers. The primary statistical endpoint for the study is diagnosis of in-breast tumor recurrence (IBTR). Regional and distant failures and death prior to IBTR will be treated as competing risks. Contralateral breast and non-breast secondary primary cancers will not be considered as competing risks. Secondary endpoints include distant disease-free interval, recurrence-free survival and overall survival.

**Progress:** This protocol received final approval in June 2006; however, enrollment was suspended in January 2007, pending approval/certification from the RTOG on Radiation Oncology Service's partial breast irradiation therapy plans. MAMC investigators never felt comfortable recruiting high risk patients to receive the planned study therapy; therefore, the protocol was terminated once only high risk patients could be enrolled. No work occurred on this protocol during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205134	<b>Status:</b> Ongoing
<b>Title:</b> Clinical Trial and Retrospective Review to Determine the Sensitivity and Specificity of Iminodiacetic Acid Scintigraphy for Fibrolamellar Carcinoma		
<b>Principal Investigator:</b> CPT David C. Semerad, MC		
<b>Department:</b> Radiology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Antonio G. Balingit, MC; COL (Ret) Jerome L. Billingsley, MD; LTC John D. Statler, MC		
<b>Start - Completion:</b> 11 Jan 2006 - Jul 2009	<b>Funding:</b> Nuclear Medicine	<b>Periodic Review:</b> 2 Jan 2008

**Study Objective:** To determine the sensitivity and specificity of iminodiacetic acid (IDA) scintigraphy for the detection of fibrolamellar carcinoma presenting as a solitary liver mass with a central scar on CT examination.

**Technical Approach:** Patients at MAMC who have a solitary liver mass with a central scar on CT will undergo IDA scintigraphy in addition to the standard diagnostic algorithm. It is estimated that 12 patients will be studied at MAMC over a 4-year period. The study protocol will also be submitted to IRBs at WRAMC and BAMC. A retrospective analysis of histologically-confirmed FLCs with IDA scintigraphy findings will also be conducted at MAMC, WRAMC, and BAMC. The goal number of total subjects is 80. The sole variable is radiopharmaceutical uptake of the lesion. Data analysis is solely descriptive, i.e. establishing the sensitivity and specificity of IDA scintigraphy for FLC.

**Progress:** This protocol remains ongoing. The AFIP and Armed Forces Tumor Registry have been contacted in an effort to identify cases of fibrolamellar carcinoma. That search is in progress. No patients with this rare tumor have been identified at MAMC over the past year.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207079	<b>Status:</b> Ongoing
<b>Title:</b> Clinical Trial to Determine the Accuracy of D-Dimer for Resolution of Acute Pulmonary Embolism		
<b>Principal Investigator:</b> CPT David C. Semerad, MC		
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Vincent Mysliwicz, MC; MAJ Mohammad Naeem, MC; CPT Charles A. Kitley, MC		
<b>Start - Completion:</b> 25 Jun 2007 - Nov 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to determine the sensitivity and specificity of D-Dimer for the detection of persistent pulmonary thromboembolism as depicted by CT pulmonary angiography (CTPA).

**Technical Approach:** MAMC Patients diagnosed as having a pulmonary embolism on CTPA , and having completed appropriate anticoagulation therapy (i.e., six months for PE due to identifiable risk factors and twelve months for patients with idiopathic PE), through the Coumadin Clinic will undergo repeat CTPA and D-Dimer within one month of anticoagulation completion. It is estimated that 80 patients will be studied over a 20 month period. Data analysis is solely descriptive. The goal of the study is to prove that a negative D-dimer signifies resolution of the PE, thus, potentially important information regarding the need for further anticoagulation could be obtained with a simple lab test.

**Progress:** This greater than minimal risk protocol was initially approved by the IRB 27 March 2007, and received final approval 25 June 2007. Protocol documents were released to the study staff on 6 August 2007. No subject enrollment reported in FY07.



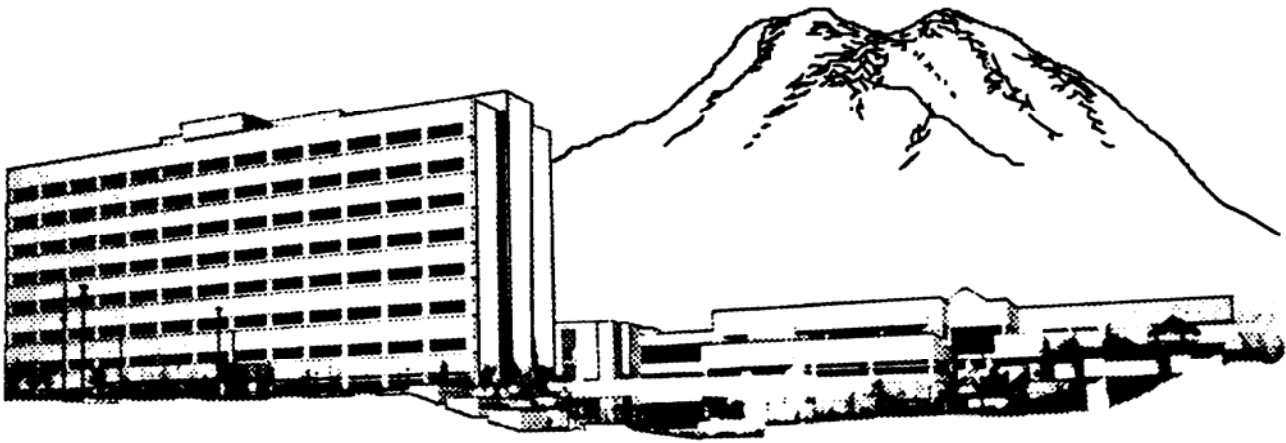
### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205051	<b>Status:</b> Completed
<b>Title:</b> Carotid Stenosis: Digital Subtraction Angiography, Magnetic Resonance Angiography, and the Evolution of Preoperative Evaluation		
<b>Principal Investigator:</b> LTC John D. Statler, MC		
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Joseph A. Ronsivalle, MC; CPT Christopher S. Johnson, MC; CPT Vance Y. Sohn, MC; LTC Benjamin W. Starnes, MC; COL (Ret) Charles A. Andersen, MD; Billinda Tatum, RN, CCRC; Leslie B. Schoneman, PA-C		
<b>Start - Completion:</b> 7 Jun 2005 - Mar 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 23 Feb 2007

**Study Objective:** This study will serve as a validation that magnetic resonance angiography (MRA) is no worse than catheter angiography in the evaluation of atherosclerotic disease of the carotid arteries.

**Technical Approach:** All adult MAMC healthcare beneficiaries referred for carotid arteriography (DSA) from vascular surgery clinic will be eligible for participation. If a patient agrees to be enrolled in the study, he/she will be consented during the visit to the vascular surgery clinic. The subject will be scheduled for DSA and MRA at the same time and will undergo both of these exams in the most expeditious order possible. Once the exams have been completed, each subject's DSA will be performed, reviewed and interpreted by one radiologist, and the MRA will be reviewed and interpreted by the other radiologist. The radiologist interpreting the MRA will be blinded to the results of the DSA, and vice-versa. Findings will be recorded on the data sheet. A general comment will be made on the quality of each exam. The images will be evaluated for percent stenosis of the common and internal carotid arteries using NASCET criteria (12) and measured by imaging software. Findings will be made based on standardized imaging criteria. Findings which may alter patient management (near occlusion, plaque ulceration, etc.) will be catalogued. At the conclusion of the review of the MRA and DSA, the results for each subject will be compared. Each subject will receive a grade with respect to the concordance of the two exams. A grade of "no difference" indicates that MRA and DSA concurred with respect to percent stenosis (+ - 10%) of internal and common carotid, and that there was no difference in detection of findings which would alter patient management. A grade of "minor difference" indicates discordance between MRA and DSA with respect to stenoses or associated findings, but that these discrepancies would not affect the decision to operate or the operative approach. A grade of "major difference" indicates discordance between MRA and DSA which would alter patient management or operative approach (discordant stenosis category, associated findings which would alter surgical management).

**Progress:** This protocol was reported as completed in June 2007, when the PI left MAMC. Two subjects were enrolled but did not provide enough data to draw conclusions. No adverse events were reported.



## **Detail Summary Sheets**

Special Forces Group, Fort Lewis

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206018	<b>Status:</b> Ongoing
<b>Title:</b> 1st Special Forces Group (Airborne) Instructing Combat Trauma Management to Trainees		
<b>Principal Investigator:</b> COL Eric P. Wendt		
<b>Department:</b> Special Forces		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Lane A Hansen; Frank J. Newton		
<b>Start - Completion:</b> 13 Jul 2005 - Jul 2008	<b>Funding:</b> 1st Special Forces Group (Airborne)	<b>Periodic Review:</b> 12 Sep 2007

**Study Objective:** To allow SOMO instructors to train SOMNCOs in methods of teaching selected volunteers to perform lifesaving medical procedures and to recognize the indication for these procedures.

**Technical Approach:** CTM training is conducted in a simulated battlefield on a multiple wounded patient. The medic acting as Student-Trainer must teach accurate assessment and resuscitation of the patient. The student-Trainer must instruct the trainees in how to treat the wounds in a timely manner. The Student-Trainer will begin by demonstrating to the Instructor-Trainer how to perform a preliminary physical examination of the animal subject in order to determine whether the animal can safely tolerate the physiologic demands of general anesthesia, wounding, and resuscitation. The animal is then placed under general anesthesia by the Student-Trainer (under supervision of the Attending Veterinarian) using intravenous and/or inhalant anesthetic agents. When the animal has reached the appropriate level of anesthesia, the Student-Trainer inflicts simulated battlefield injuries. The animal is transported to a Combat Trauma Management scenario for resuscitative procedures.

The Trainees/Volunteers will immediately be summoned with the battlefield call of "MEDIC", "Corpsman" or a regionally appropriate foreign language equivalent title, and will then begin an exercise comprising primary and secondary assessments, resuscitation, wound treatment, and casualty evacuation. The Special Operations Medic acting as the Student-Trainer will be graded on how successfully he teaches, coaches and mentors the Volunteers in recognizing life-threatening conditions and in initiating immediate and appropriate medical treatment.

**Progress:** The Laboratory Animal Resources Service supported 14 Special Forces training labs which provided training to 179 Special Forces medics and support personnel.

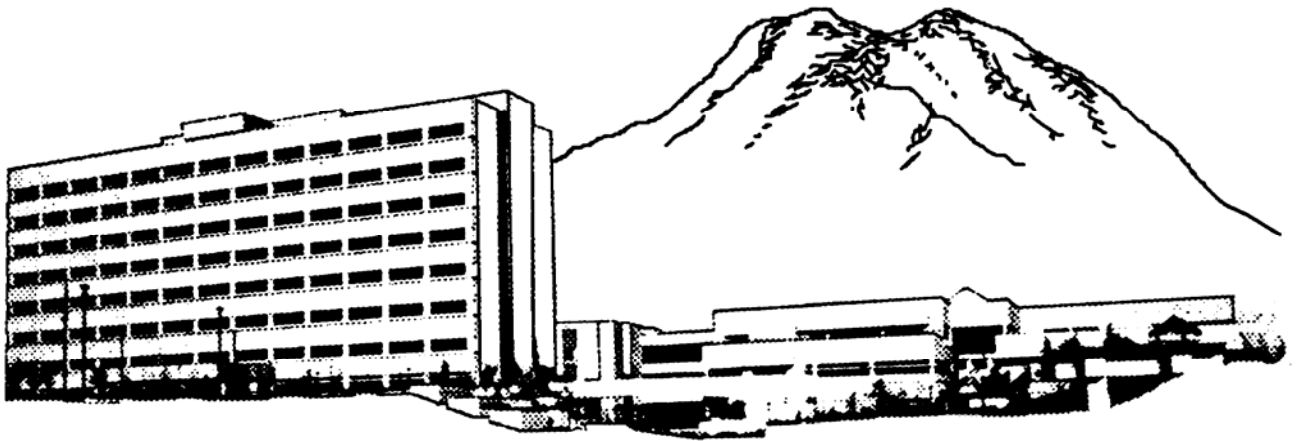
### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206106	<b>Status:</b> Ongoing
<b>Title:</b> 1st Special Forces Group (Airborne) Combat Trauma Management Procedures Training for Special Forces Medical Personnel		
<b>Principal Investigator:</b> COL Eric P. Wendt		
<b>Department:</b> Special Forces		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Lane A Hansen; Frank J. Newton		
<b>Start - Completion:</b> 13 Jul 2005 - Jul 2008	<b>Funding:</b> 1st Special Forces Group (Airborne)	<b>Periodic Review:</b> 12 Sep 2007

**Study Objective:** Trauma is the leading cause of death among American ages 1-44. The purpose of this training exercise is to teach critical trauma management and resuscitative tasks. This exercise emulates, in part, the instruction in the Special Forces Medical Sergeant's/Advanced Special Operations Combat Medic course. It is intended to teach lifesaving procedures under simulated tactical scenarios which are stressful, challenging and austere.

**Technical Approach:** Combat management training is conducted in a simulated battlefield on a multiply wounded patient. The student must accurately access the patient, resuscitate him, and then treat the wounds in a timely manner. The student will perform a preliminary physical examination of the animal subject and determine that the subject can safely tolerate the physiologic demands of general anesthesia, wounding and resuscitation. The animal is placed under general anesthesia using intravenous anesthetic agents. When the animal has reached the appropriate level of anesthesia, an instructor inflicts simulated battlefield injuries. The animal is transported to a Combat Trauma Management scenario for resuscitative procedures. The student is immediately summoned and begins an exercise comprised of primary and secondary assessments, resuscitation, wound treatment and casualty evacuation. The successful student will recognize life threatening conditions and initiate immediate and appropriate medical treatment. The protocol is also used to sustain medical skills of those who have already graduated from the JSOMTC or its predecessor, the "Med Lab." This specifically applies to the Special Forces Medical Sergeant's Advanced Non-Commissioned Officer's Course Combat Trauma Management Procedures Training or the Special Operations Forces Medical Skills Sustainment Program.

**Progress:** The Laboratory Animal Resources Service supported 14 Special Forces training labs which provided training to 179 Special Forces medics and support personnel.



## Detail Summary Sheets

Cardiothoracic Service, Department of  
Surgery

### Detail Summary Sheet

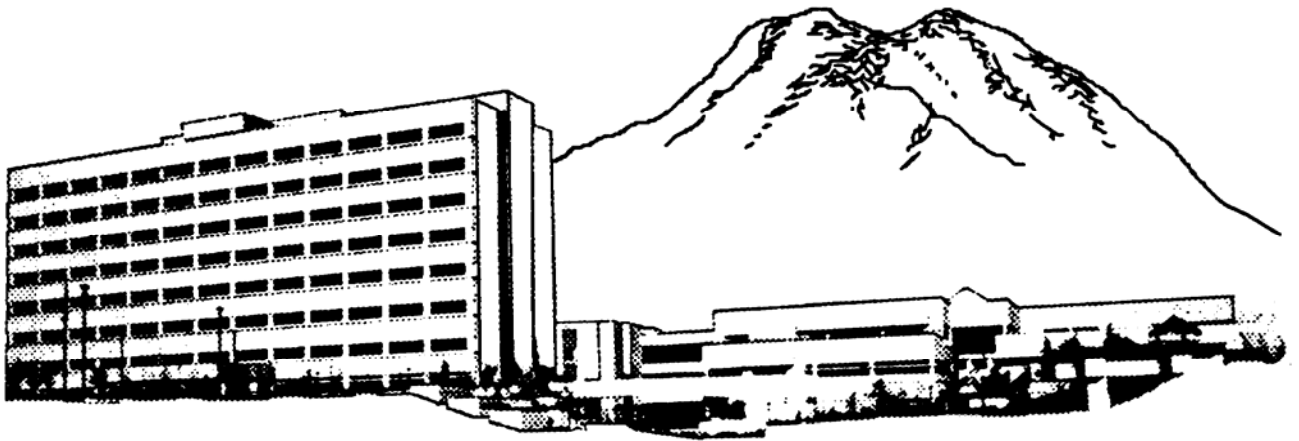
<b>Date:</b> 30 Sep 07		<b>Number:</b> 207070	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized, Double-blind, Placebo-controlled study of Glypromate in Patients Undergoing Cardiopulmonary Bypass Surgery (SNUG-2)			
<b>Principal Investigator:</b> LTC Keith A. Havenstrite, MC			
<b>Department:</b> Surgery/Cardiothoracic			<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Jerome M. McDonald, MC; LTC Michael S. Meyer, MC			
<b>Start - Completion:</b> 21 May 2007 - Mar 2012	<b>Funding:</b> Hesperion US, Inc. via Henry M. Jackson Foundation		<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective of this study is to evaluate the efficacy of Glypromate compared to placebo in the reduction of cognitive decline in patients undergoing CABG surgery and/or valve replacement/ repair with cardiopulmonary bypass (CPB).

The secondary objectives are to (1) evaluate the effect of Glypromate compared to placebo on the incidence of stroke and transient ischemic attack (TIA) after CABG surgery and/or valve replacement/ repair with cardiopulmonary bypass (CPB), (2) evaluate the effect of Glypromate compared to placebo following CABG surgery and/ or valve replacement/ repair with CPB on the change in domain and individual cognitive test performance, and (3) evaluate the effect of Glypromate compared with placebo following CPB surgery on the incidence of adverse events up to the 6-8 week follow-up.

**Technical Approach:** This is a randomized, double-blind, placebo controlled study of Glypromate versus placebo in subjects who are scheduled for non-emergent CABG or valve repair/ replacement with CPB. Eligible subjects will be > 50 years of age, male or female of non-childbearing potential, who are capable of completing the neurological, cognitive and mood assessments. Consent will be obtained by the PI or sub-I during a scheduled pre-surgical exam. Subjects will receive a 4-hour IV infusion of study drug or placebo starting at the time of protamine administration. Subjects will be followed for concomitant medications and adverse events for 14 days or until discharge from the hospital. Follow-up assessments will be completed at the end of study visit at Week 6-Week 8.

**Progress:** This greater than minimal risk protocol was initially approved by the IRB on 27 February 2007, and received final approval 21 May 2007. Protocol Version 2 dated 11 May 2007, and an updated IDB version 10.0 dated 26 April 2007 were submitted in July 2007, and the amended protocol approved by the IRB. Protocol documents were released to the study staff on 10 August 2007, and one subject was enrolled in FY07.



## Detail Summary Sheets

General Surgery Service, Department of  
Surgery

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203090	<b>Status:</b> Completed
<b>Title:</b> The Association Of Elevated C-Reactive Protein With Presence And Degree Of Carotid Stenosis		
<b>Principal Investigator:</b> CPT Zachary M. Arthurs, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Philip S. Mullenix, MC; COL (Ret) Charles A. Andersen, MD; Leslie B. Schoneman, PA-C; MAJ Garth S. Herbert, MC; CPT Craig S. See, MC; LTC Benjamin W. Starnes, MC; CPT Katharine E. Wolcott, MC; CPT Daniel G. Cuadrado, MC; MAJ Allen D. Rubin, MC		
<b>Start - Completion:</b> 1 Jul 2003 - Dec 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 28 Aug 2006

**Study Objective:** Evaluate the association between serum CRP levels and the presence and degree of carotid stenosis.

**Technical Approach:** This is a prospective observational concurrent cohort study evaluating the potential relationship between serum C-reactive protein levels and the presence and degree of carotid stenosis. It involves two study arms, a cohort with carotid stenosis, and one without, as defined by bilateral carotid duplex ultrasound. The study involves two phases. Phase I will (1) compare the measured initial CRP means between the two cohorts, and (2) correlate the amount of elevation of CRP with the measured degree of carotid stenosis. Phase II is a longitudinal study designed to stratify increased risk of progression of carotid disease or adverse neurologic outcomes using odds ratios generated from measured CRP quartile means.

**Progress:** Protocol reported as completed during FY07. Results: During the study period, 271 patients completed study requirements with a mean follow-up of 37(+6) months. Initial duplex examination revealed 114 (41 %) of patients had 1-15%, 94 (35%) had 16-49%, and 63 (23%) had 50-79% stenosis of the carotid bifurcation. Sixty-three patients (23%) demonstrated progression of disease by ultrasound examination, 27(10%) progressed to carotid endarterectomy, and 3(1 %) experienced a stroke during follow-up. Mean CRP levels were higher among patients that progressed on duplex examination (6.7+-1.28 vs. 4.6+-0.4 mg/dl, P<0.05). Kaplan-Meier analysis revealed a significant difference in freedom from progression of carotid artery disease for patients with 4th quartile CRP levels (Figure 1). Adjusting for age, diabetes, hypertension, LDL, smoking, coronary artery disease, baseline carotid artery disease, and statin therapy, 4th quartile CRP was independently associated with disease progression (OR 1.8, 95% CI; 1.03-2.99, p<0.05).

**Conclusions:** CRP levels are a predictor of patients with carotid artery stenosis who are more likely to progress on serial duplex examination. In addition, it may provide additional diagnostic value for evaluation and follow-up of patients with borderline lesions identified by duplex exam.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206032	<b>Status:</b> Completed
<b>Title:</b> Colonic Ischemia Following Abdominal Aortic Aneurysm Repair-- Open vs. Endovascular Approaches		
<b>Principal Investigator:</b> CPT Zachary M. Arthurs, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Scott R. Steele, MC; LTC Matthew J. Martin, MC; MAJ Philip S. Mullenix, MC; LTC Benjamin W. Starnes, MC; COL (Ret) Charles A. Andersen, MD; COL Kenneth S. Azarow, MC		
<b>Start - Completion:</b> 14 Dec 2005 - Dec 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 23 Oct 2007

**Study Objective:** To determine if there are any differences in colonic ischemia complications following abdominal aortic aneurysm repair using an open versus an endovascular approach and determine any peri-operative factors which may contribute to that difference.

**Technical Approach:** This is a retrospective review comparing a consecutive series of endovascular repairs for abdominal aortic aneurysms. A chart review of all cases of the endovascular approach will be performed and results compared to historical controls of the open approach. Open patients will be consecutive patients coming from the time period just preceding the startup of the endovascular approach. ORMA will be used to generate the patient names for each of the two methods to perform the chart review.

**Progress:** This protocol was reported as completed during FY07. Identified 89,967 admissions for aortic aneurysm repair (mean age 69.9 years). Open repair was performed in 51,671 cases (58%) and was associated with younger patients (67 vs. 73 years), longer length of stay (12 vs. 4 days), increased total charges (\$89,500 vs. \$64,453), increased need for skilled aftercare (40% vs. 17%) and increased mortality (11.2% vs. 2%; all  $P < 0.01$ ). Ischemic colitis occurred in 2.2% (1,941 cases), and was significantly higher following open repairs (3.2% vs. 0.7%,  $P < 0.001$ ). Independent predictors of developing ischemic colitis were female sex (odds ratio [OR] = 1.2), rupture on presentation (OR = 1.6), open repair (OR = 2.3), and higher disease severity (OR = 3.1; all  $P < 0.001$ ). The development of ischemic colitis was a strong independent predictor of mortality (adjusted OR = 2.4,  $P < 0.001$ ).

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206123	<b>Status:</b> Completed
<b>Title:</b> Renovascular Hypertension: A Retrospective Analysis of Renal Artery Stenting Outcomes		
<b>Principal Investigator:</b> CPT Zachary M. Arthurs, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Daniel G. Cuadrado, MC; CPT Vance Y. Sohn, MC; COL (Ret) Charles A. Andersen, MD; LTC Benjamin W. Starnes, MC		
<b>Start - Completion:</b> 13 Sep 2006 - Dec 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objectives of this study are to establish the impact of renal artery stenting on patients hypertension control and on their renal function, and determine the natural history of patients that have not been treated with stenting of the renal arteries.

**Technical Approach:** To perform a retrospective review of inpatient and outpatient records for patients that were presented at a Multidisciplinary Renovascular Conference, which included nephrologists, interventional radiologists, and vascular surgeons. Patients with atherosclerotic renal artery disease are to be included between January 2001 and June 2006. Patients presented at this conference were referred by nephrologists for multiple medication hypertension, worsening renal function, or congestive heart failure. The multidisciplinary team evaluated each patient for potential renal artery stenting, and as a result there was a cohort of patients that were followed with medical management. Reasons patients were not offered stenting include: inadequate anti-hypertensive regimen, poor patient compliance, acute medical conditions, resistive indice >0.80, and lesions that were <70% stenosis. A retrospective chart analysis will be performed of inpatient and outpatient up records. The patients that were not offered stenting will be used as a comparison against the population that underwent stenting. While not an adequate control since these patients were selected by the conference, they will provide a comparison for the natural history of worsening renovascular disease. Initial screening of the renal vascular bed is performed with duplex ultrasound criteria, and if the study was noncontributory, magnetic resonance angiography (MRA) or computed tomographic angiography (CTA) was performed as a confirmatory test.

**Progress:** This protocol was completed during FY07, with 50 charts reviewed; 41 found to have usable information. Median follow-up was 14.9 months. Conclusions: Blood pressure is only transiently responsive. Bilateral disease may have a more durable response. Renal Artery Stenosis significantly slows renal function decline.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207007	<b>Status:</b> Completed
<b>Title:</b> Panniculectomy Following Massive Weight Loss After Bariatric Surgery: A Descriptive Analysis		
<b>Principal Investigator:</b> CPT Zachary M. Arthurs, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Tommy A. Brown, MC; CPT Vance Y. Sohn, MC		
<b>Start - Completion:</b> 20 Oct 2006 - May 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to evaluate the incidence of panniculectomy among patients undergoing bariatric procedure and to determine the complication profile of this procedure.

**Technical Approach:** This is a retrospective review of consecutive panniculectomies performed at MAMC since 2002. Data will be collected with respect to pre-operative variables, operative data points, as well as post-operative complications, using an Excel spreadsheet to collect and organize the data.

**Progress:** Work under this minimal risk protocol was completed during FY07, with 126 records reviewed. Of those records, 96% of patients were female, mean age 42 +/- 12. Complication rates were: seroma 17%, hematoma 13%, surgical site infection 17%, transfusion 6%, skin breakdown/necrosis 11%, and re-exploration 11%; with 40% of patients experiencing a complication. Patients report subjective improvement, and an increasing number of patients are returning for body contouring procedures. Even though this population has experienced significant weight loss, they are still at an increased risk for post-operative complications. Maximal reduction in BMI should be stressed to these patients in order to reduce the risk of complications following panniculectomy.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207112	<b>Status:</b> Ongoing
<b>Title:</b> Technical Success, Conversion, and Complications in Patients Undergoing Totally Percutaneous Aortic Aneurysm Repair With and Without Ultrasound-Guided Access		
<b>Principal Investigator:</b> CPT Zachary M. Arthurs, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD		
<b>Start - Completion:</b> 25 Jul 2007 - Jun 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this protocol is to determine the impact ultrasound-guided access on groin complications for totally percutaneous aortic aneurysm repair.

**Technical Approach:** All consecutive patients undergoing totally percutaneous closure of large-bore-sheath (>12F) access sites with a suture-mediated closure device will be included. The cohort will be stratified into two groups by access technique. Group A underwent femoral access without the use of ultrasound guidance, and Group B underwent femoral access using ultrasound guidance with the intent of needle access in the common femoral artery just above the femoral bifurcation. Patient variables will be evaluated, and outcome measures will include technical success, requirement for conversion to open repair, and access-related complications. Recorded conversions will only include those related to access closure technique.

**Progress:** This minimal risk protocol received final approval by the Expedited Review Committee, effective 25 July 2007. No records were reviewed during FY07.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207113	<b>Status:</b> Completed
<b>Title:</b> Endovascular Aneurysm Repair: The Impact of Transrenal Fixation on Renal Function		
<b>Principal Investigator:</b> CPT Zachary M. Arthurs, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD		
<b>Start - Completion:</b> 25 Jul 2007 - Dec 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this protocol is to determine the impact of transrenal fixation on endovascular aneurysm repair.

**Technical Approach:** This will be a retrospective chart review of clinical data for all patients with a transrenal endograft, which will be analyzed with follow-up labs, radiographic, and other clinical notes. Patient demographic factors will be recorded as well as underlying renal disease. Demographic variables include age, sex, hypertension, hyperlipidemia, diabetes mellitus, smoking history, coronary artery disease, carotid artery disease, peripheral vascular disease, and known renal insufficiency. Follow-up variables will include the number of CT scans obtained and total intravenous contrast given during this period. Axial imaging will be reviewed for renal size, renal cortical thickness, and new renal infarctions. The primary endpoint will be the development of new chronic renal insufficiency as defined by Cr >1.5mg/dl. It is arguable that other estimates of renal function (Cockcroft Formula) may better serve as a marker of renal impairment, but in those formulas, several of the variables are constants during the follow-up period. Age changes very little, and weight, race, sex are all constants. Therefore, the creatinine level is the only aspect that changes with short 1-3 year follow-up periods.

**Progress:** This minimal risk protocol received final approval by the Expedited Review Committee, effective 25 July 2007. Results: During the study period, 77 EVAR's were performed; 63 met inclusion criteria. Mean pre-procedural observation was 36(+ 24) months and mean follow-up was 11.7(+ 9) months. Transient acute renal insufficiency occurred in 15%, whereas renal impairment occurred in 30% of patients at last follow-up. 65% experienced a worsening inverse creatinine slope after EVAR. Stratifying the population based on the development of renal impairment, univariate analysis revealed significance ( $P < 0.05$ ) to exist in the presence of intrinsic nephropathy, last creatinine, 1/Cr slope decline, and follow-up. Subjecting the population to logistic regression analysis, the presence of intrinsic nephropathy and worsening creatinine slope were independent predictors of renal impairment during the follow-up period ( $P < 0.05$ ).

**Conclusions:** A significant proportion of patients after EVAR experience renal impairment at follow-up period, and an even higher percentage of patients have a decrease in their inverse creatinine slope. Renal sparing adjuncts should continue to be utilized in patients with known intrinsic nephropathy. Only half of patients with worsening inverse creatinine slope developed renal impairment during the follow-up period, longer follow-up is needed to identify the magnitude of late renal impairment.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205075	<b>Status:</b> Ongoing
<b>Title:</b> Operation Iraqi Freedom Combat Trauma Database from the 31st Combat Support Hospital, Baghdad, Iraq		
<b>Principal Investigator:</b> MAJ Alec C. Beekley, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC James A. Sebesta, MC; LTC Tommy A. Brown, MC; COL (Ret) Charles A. Andersen, MD; COL Kenneth S. Azarow, MC; CPT Randy J. Kjorstad, MC; CPT Zachary M. Arthurs, MC; CPT Daniel G. Cuadrado, MC; CPT Troy P. Houseworth, MC; CPT Rebecca M. McGuigan, MC; MAJ Philip S. Mullenix, MC		
<b>Start - Completion:</b> 6 May 2005 - Jan 2010	<b>Funding:</b> DCI	<b>Periodic Review:</b> 7 May 2007

**Study Objective:** To retrospectively review the recorded combat trauma, burn, pediatric, vascular, elective, and humanitarian surgical activities collected at the 31st Combat Support Hospital, Baghdad, Iraq between 1 Jan 04 and 31 Dec 04 that was recorded in an existing, secure, and confidential database for purposes of (1) continuous quality analysis/improvement of military surgical care in combat and (2) academic publication and presentation.

**Technical Approach:** Retrospective database (spreadsheet) review. Specific study questions (spreadsheet queries) will be submitted as specific addendums. Examples of typical study questions of interest might include (descriptive data analysis of existing spreadsheet only): Incidence of military admissions compared to civilian admissions at a large CSH. Primary and secondary surgical procedures performed compared between various patient subsets. Percentage of patients requiring ICU admissions compared between various patient subsets. Mortality rate of patients compared between various patient subsets. Length of ICU and Hospital stay compared between various patient subsets. Admission laboratory data to include vitals, Glasgow coma score, complete blood count, arterial blood gas with base deficit, and blood products administered. Distribution of primary and secondary cause of injury compared between various patient subsets. Incidence of damage control operations and operative times compared between various patient subsets. Injury severity scores compared between various patient subsets. Cause of death compared between various patient subsets. Proportion of patients that received level one or level two care as compared between various patient subsets.

**Procedures:** Dr. Beekley (PI) and Dr. Beekley alone will create code list for patient name/SSN. He will then permanently delete PHI (name/SSN/PHI) field columns from Excel spreadsheet and replace with code list number. Then he will permanently destroy all records of name/SSN/PHI leaving only the code list number. Even the PI will not have PHI after that point, and none of the AI's will ever see PHI. Decide on a specific study question of interest for database query. Submit addendum to this protocol to MAMC IRB with specific question and variables to be analyzed. Cut and paste pertinent study data from secure de-identified computerized Excel spreadsheet file into new spreadsheet specific to that problem (delete irrelevant fields, calculate new variables from existing data). Maintain the new spreadsheet in same secure, de-identified manner using existing code list system.

**Analyze data.** Due to the nature of the database and fields available, these statistical analyses employed will be straightforward, descriptive, and observational in nature, in general designed to compare various subset cohorts identified within the total data set. Report and present data in entirely de-identified fashion (no names, patient numbers, patient specific data or identifiable injury pattern, etc - typical chart review reporting). Destroy code list specific to that study question and destroy all hard copies if any.

**Progress:** Information on 166 cases has been entered into the database. Data analysis continues. Several papers have been written and submitted, and others are in various stages of preparation. This protocol remains ongoing.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207009	<b>Status:</b> Ongoing
<b>Title:</b> Influence of Post-Bariatric Surgery Weight Loss on Endothelial Progenitor Cells, Inflammation, and Oxidative Stress in the Morbidly Obese		
<b>Principal Investigator:</b> CPT Lionel R. Brounts, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Niten N. Singh, MC; CPT Jason T. Perry, MC; COL (Ret) Charles A. Andersen, MD; LTC Benjamin W. Starnes, MC; LTC Matthew J. Martin, MC		
<b>Start - Completion:</b> 20 Dec 2006 - Sep 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 9 Oct 2007

**Study Objective:** The objectives of this study are to identify abnormalities in (1) endothelial progenitor cell number and function in patients with morbid obesity and correlate correction of those abnormalities with resolution of obesity-related comorbid illness following bariatric surgery, (2) inflammatory mediators and oxidative stress in patients with morbid obesity prior to surgery and determine if these abnormalities resolve following surgery, and (3) vascular health in patients with morbid obesity as measured by brachial artery reactivity and determine if these abnormalities resolve following surgery.

**Technical Approach:** Thirty patients meeting inclusion criteria will be offered entry into the study and study registry; fifteen bariatric surgery patients with no obesity-related comorbidity and fifteen bariatric surgery patients who have one or more obesity-related comorbidity). Pre-operatively and at six and twelve months post-operatively, medical histories will be reviewed for current medication, occurrence of surgical complications, and development or resolution of comorbid illness (including CVD, CAD, PVD, DM, and hypertension). At the same time points, blood pressure, height, weight, BMI, and waist and hip circumference measurements will be obtained. Pre-operatively and at twelve months post-operatively brachial artery flow-mediated dilatation will be assessed. To evaluate endothelium independent vasodilatation, sublingual nitroglycerin (0.4 mg) will be administered. Three minutes after administration, brachial artery diameter will be assessed. Patients known to be allergic to nitrates will not participate in this portion of the examination. Percent flow-mediated dilatation will then be calculated by taking the difference between the pre- and post-cuff placement arterial diameters divided by the pre-cuff placement diameter. Patients will undergo fasting phlebotomy (approximately 100 mL blood at each draw) and provide a urine sample on the day of their pre-operative visit and at six and twelve months post-operatively. A portion of the blood drawn will be sent to the MAMC clinical laboratory for routine pre- and post-operative evaluation and the remainder used for further analyses: EPC isolation; EPC culture and quantification: Late outgrowth cells, EPC characterization; EPC functional analysis: Migration assay, Matrigel tubule assay; Serum inflammatory and vasoactive mediator assay, Serum oxidized LDL assay, and Urine 8-epi-PGF2alpha assay.

**Progress:** This greater than minimal risk protocol received initial IRB approval 24 October 2006, and final approval was received 20 December 2006. No patients have been enrolled, as the PI continues to finalizing the lab procedures. So far the PI has been able to isolate mononuclear cell and quantify EPC cells by fluoroscopy, colony forming units and antibody staining. Complications have occurred with the flow cytometer; the PI is awaiting repairs to run samples. PI has also been growing cells for further analysis of migration and tubule formation.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207031	<b>Status:</b> Ongoing
<b>Title:</b> Prospective Randomized Control Study of Vacuum Assisted Closure Device for therapy in pilonidal disease		
<b>Principal Investigator:</b> CPT Lionel R. Brounts, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Daniel G. Cuadrado, MC; MAJ Scott R. Steele, MC		
<b>Start - Completion:</b> 18 Apr 2007 - Dec 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 11 Dec 2007

**Study Objective:** Compare the rate of wound healing between the vacuum-assisted closure device (KCI Wound Vac) to conventional moist dressings in the treatment of pilonidal disease following surgical intervention.

**Technical Approach:** Subjects with pilonidal disease requiring operative incision and drainage will be enrolled. They will be randomly assigned to either wound vac therapy or conventional wet-to-dry saline dressings. The wound will be photographed prior to surgery and immediately after specimen removal. Wound dimensions will be measured intra-operatively and the grams of tissue removed will be recorded. Both groups will be seen twice a week in the General Surgery Clinic until wound closure, defined as complete re-epithelialization. Those in the wound vac group will have there vac changed at their clinic appointments. The conventional dressing arm will be instructed on self-wound care and change their dressings three times a day. Wounds will be examined by a physician at each clinic visit and photographed once per week. The wound dimensions will be measured at each appointment. In the vac group, at the discretion of the treating attending physician, once the wound has contracted to the point where a vac can no longer be successfully applied, the subjects will be converted to conventional dressings. Follow-up will continue until wound closure.

**Progress:** This greater than minimal risk protocol was initially approved by the IRB 12 December 2006, and final approval received 18 April 2007. Two subjects have been randomized to the VAC treatment so far with no complications. Subject enrollment continues.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207126	<b>Status:</b> Ongoing
<b>Title:</b> Influence of Post-Bariatric Surgery Weight Loss on Lower Extremity Vein Hemodynamics		
<b>Principal Investigator:</b> CPT Lionel R. Brounts, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD; LTC James A. Sebesta, MC; MAJ Niten N. Singh, MC		
<b>Start - Completion:</b> 24 Sep 2007 - 10/08	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To identify abnormal vein hemodynamics in lower extremities correlated with varicose veins and changes of these hemodynamics associated with possible resolution of varicose veins following bariatric surgery.

**Technical Approach:** Patients with morbid obesity share many comorbidities including lower extremity vein disease. Although obesity has been associated with vein disease, a clear etiology has not been found. There is evidence that varicose veins improve after weight loss from bariatric surgery, but again no mechanism has been explored. With the use of air plethysmography (APG) and color-flow duplex ultrasonography measurements can be made pre and post surgery to find a correlation between the hemodynamics pre-surgery and pre-weight loss compared to post surgery and post-weight loss.

**Progress:** This minimal risk protocol received final approval by the Expedited Review Committee, effective 24 September 2007.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 205112	<b>Status:</b> Terminated
<b>Title:</b> RTOG 0412 / SWOG S0332, Phase III Randomized Trial of Preoperative Chemotherapy Versus Preoperative Concurrent Chemotherapy and Thoracic Radiotherapy Followed By Surgical Resection and Consolidation Chemotherapy in Favorable Prognosis Patients with Stage IIIA (N2) Non-Small Cell Lung Cancer			
<b>Principal Investigator:</b> LTC Tommy A. Brown, MC			
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC James A. Sebesta, MC; MAJ Alec C. Beekley, MC; COL John B. Halligan, MC; LTC William B. Reece, MC; MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; LTC David E. McCune, MC			
<b>Start - Completion:</b> 15 Dec 2005 - Aug 2010		<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 10 Jul 2006
<b>Study Objective:</b> (1) To prove that the preoperative regimen, consisting of thoracic radiation therapy given concurrently with chemotherapy followed by surgical resection, results in a significant improvement in overall survival compared to preoperative chemotherapy alone followed by surgical resection, with both arms receiving postoperative consolidation therapy (2) comparison of progression-free survival, median survival time, and toxicity and response rates (clinical and pathologic) in both treatment arms (3) evaluate the correlation of the pCR with the disease-free and overall survival (4) to investigate the association of DNA damage repair genes (ERCC1 and XRCC1), microtubule- related proteins (TUBB-III and MAP4), and shed tumor DNA with patient responses and outcomes to the platinum/taxane/radiation therapy in this trial (5) to employ MALDI-TOF proteomic analysis of tumor and serum to identify protein profiles associated with response to therapy and prognosis (6) to evaluate the role of FDG-PET post-therapy in predicting long-term outcome, as well as pathological response both in the tumor and in the mediastinal lymph nodes (7) to assess patient-reported functional status as an endpoint with potentially relevant differences between the two arms and (8) to determine the impact of co-morbid conditions on survival.			
<b>Technical Approach:</b> This study is a randomized trial of preoperative chemotherapy versus concurrent chemoradiation followed by resection and consolidation in patients with Stage IIIA NSCLC. Up to 547 subjects will be enrolled in this study over a period of approximately four years with up to 6 subjects a year expected to enroll at MAMC. Patients in the chemotherapy arm will receive induction therapy with CDDP at 75 mg/m2 on Days 1 and 22. Patients on the chemoradiation arm will receive CDDP at 50 mg/m2 on days 1, 8, 22, and 29, with concurrent radiation therapy delivered 5 days a week for a total of 50.4 Gy. Both groups will be reevaluated 3 to 5 weeks after induction, and then continue to resection if there is no progression of disease. Patients in both arms will receive consolidation chemotherapy 4 to 6 weeks after surgery. Consolidation will consist of Docetaxel, 75 mg/m2 on Days 1, 22 and 43, with growth factor support 24 hours after each chemo dose. Randomization to either arm will be stratified based on extent of nodal involvement, nodal micro-metastases, and T stage. Follow-up visits will be done every 3 months for the first year, every 6 months for 2 years, then annually until death.			
Included within this protocol are translational research, proteomics, FDG-PET and quality of life studies. Blood and tissue samples will be submitted from biopsy and resection specimens. Copies of pre- and post-induction scans will be submitted. Some of these studies are optional, and are specifically addressed in the consent form. ERCC1, XRCC1, TUBB-III and MAP4 are all genetic markers that have been associated with susceptibility or resistance to various chemotherapy agents. Levels of these markers will be correlated with patient outcomes. Shed Tumor DNA can be detected in patient plasma, and will be examined for a response to presence or lack of tumor. Proteomic analysis by MALDI-TOF will be done to attempt to correlate several known proteomic			

patterns with patient outcome. FDG-PET data will be examined to define its usefulness in imaging the status of nodal disease in these patients.

**Progress:** RTOG closed this protocol in December 2007, due to not meeting accrual goals. No subjects enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206015	<b>Status:</b> Ongoing
<b>Title:</b> A Prospective Randomized Study Comparing Sentinel Lymph Node (SLN) Evaluation with Standard Pathological Evaluation for the Staging of Colon Carcinoma		
<b>Principal Investigator:</b> LTC Tommy A. Brown, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Alec C. Beekley, MC; LTC Robert M. Rush, MC; LTC Gregory P. Fitzharris, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 9 Jun 2006 - Oct 2010	<b>Funding:</b> DCI	<b>Periodic Review:</b> 11 Dec 2007

**Study Objective:** The objective of this trial is to define the rate of upstaging of colon carcinoma lymph node metastasis with sentinel lymph node (SLN) mapping.

**Technical Approach:** Male and female military healthcare beneficiaries over the age of 18 years presenting at the General Surgery Clinic with the diagnosis of biopsy-proven, primary, non-metastatic (Clinical Stage I,II or III) colon carcinoma will be enrolled. Subjects with colonic masses clinically consistent with colon cancer and eventually confirmed by pathology, will also be enrolled. A total of 150 patients will be enrolled; up to 20 patients per year are expected to be enrolled at MAMC. A complete history and physical examination including demographic data, co-morbid conditions, past surgical history, clinical tumor staging, American Society of Anesthesiologists classification, height and weight will be performed within one month before surgery. Pre-operative evaluation will consist of complete blood count (CBC), coagulation profile (PT/PTT), screening profile including: electrolytes, blood urea nitrogen, creatinine, pulmonary function testing, chest radiography and electrocardiogram (at the discretion of the attending surgeon). Pre-operative clinical staging will be conducted according to MAMC current standard of care and will include colonoscopy and serum carcinoembryonic antigen (CEA).

Subjects randomized to the standard histopathology arm will undergo a standard surgical resection of the colon cancer. The entire surgical specimen (colon and mesentery) will be sent to the pathologist for standard histopathological evaluation and staging of the cancer using conventional paraffin embedding, sectioning and hematoxylin and eosin staining (H&E) and microscopy. Subjects randomized to the SLN arm of the trial will undergo standard surgical resection of the colon cancer including the normal wedge of mesentery containing the draining lymphatics. Immediately following resection the surgical specimen will be stained. The investigator will dissect all blue nodes from the mesentery and submit them to pathology as separately labeled specimens (SLNs). The remaining resected colon with attached mesentery will then be sent fixed in formalin for standard histopathological evaluation of non-SLNs, as per standard of care protocol. The SLN pathology results will be made available to both the subject and the subject's physician. Subject participation will conclude with the surgical procedure. No follow-up is required for this clinical trial.

**Progress:** This protocol remains open to enrollment with two subjects enrolled during FY06, none during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206110	<b>Status:</b> Terminated
<b>Title:</b> Comparative Medical/Surgical Research and Development (Limited)		
<b>Principal Investigator:</b> LTC Tommy A. Brown, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Matthew J. Martin, MC; LTC James A. Sebesta, MC; CPT Matthew J. Eckert, MC; CPT Jason T. Perry, MC		
<b>Start - Completion:</b> 12 Jul 2006 - July 2009	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To facilitate preliminary investigations of proposed animal research models and pilot studies, as well as the practice of newly described surgical procedures on animals prior to use in human patients in an effort to refine and reduce the sacrifice of animals and enhance the quality and effectiveness of medical/surgical patient services at MAMC.

To provide uniform standards and assurances of proper animal care and use in the conduct of limited animal model development, pilot studies and surgical advancement training proposed by MAMC-affiliated medical staff.

This protocol is designed to facilitate preliminary investigative medical and surgical research and development as described below: a) Development or refinement of animal models for medical/surgical research or training. b) Limited pilot studies (animal) that are preliminary to more extensive research proposals. c) Practice of newly described surgical procedures, animal models prior to utilization in the MAMC human surgical patient population.

**Technical Approach:** The details of experimental design and general procedures will be provided in each addendum to this protocol. The MAMC/DCI veterinarian (PI) will be consulted in the development of all addenda to this protocol.

1. Proposed animal model development/refinement will be based on previously described animal models that are considered to be flawed, recognized similarities in comparative physiological/anatomical characteristics of particular animal species and humans or similarities in disease processes. Pilot studies will likewise reference applicable similarities in comparative physiological/anatomical features between proposed animal models and humans as related to the investigative question posed in the study. Practice of newly described surgical procedures will be conducted on animal species possessing the most comparable organ systems of interest, then compared to human anatomy and physiology.
2. Where applicable, animals will receive species-specific pre-anesthetic medication, anesthesia and post surgical analgesia (as applicable) as described in Section V.C.2.b., 3.a. and 7.b (1) of Technical Methods. Requirements for pre, intra and/or post-operative bio-sample (e.g. blood, urine, etc) collection or diagnostic imaging (e.g. radiography ultrasonography, etc.) will be described in Section V.C.3.b, and e. of Technical Methods in each procedure-specific addendum.
3. Procedural descriptions and post-operative care instructions will be provided in Sections V.C.2.a and b. of Technical Methods and V.D.1. and 2. of Veterinary Care in each addendum. Methods of euthanasia and study endpoints will be described in Section V.C.3.5. and 6. of the Technical Methods in each addendum.

**Progress:** One amendment was approved using four pigs for a pilot study to establish a hemorrhage model, but it was unsuccessful. No further work will be done, and the protocol will be terminated in November 2007 once the investigator's final report is submitted for IACUC review.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 202013	<b>Status:</b> Ongoing
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**Title:** Bariatric Surgery Effects on the Comorbidities of Obesity

**Principal Investigator:** COL (Ret) Preston L. Carter, MD

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** MAJ Alec C. Beekley, MC; LTC James A. Sebesta, MC; COL David M. Watts, MC; LTC Robert M. Rush, MC; Margaret I. Voelker, RN, CRC; MAJ Philip S. Mullenix, MC; COL Kenneth S. Azarow, MC; CPT Daniel G. Cuadrado, MC; CPT Katharine E. Wolcott, MC; CPT Zachary M. Arthurs, MC; COL (Ret) William E. Eggebroten, MD

**Start - Completion:**  
24 Oct 2001 - Mar 2006

**Funding:**  
DCI

**Periodic Review:**  
26 Nov 2007

**Study Objective:** To determine and compare the effectiveness of resectional and laparoscopic gastric bypass in regards to reducing the comorbidities and mortality associated with morbid obesity.

**Technical Approach:** This study is a prospective observational study to analyze the effects of resectional and laparoscopic bypass on the morbidity and mortality of morbid obesity. All patients undergoing bariatric surgery at MAMC will be included in the study. A history, examination, and labs will be done preop, 3-6-and 12 months post-op. The variables and outcomes measured will include: weight, insulin/oral hyperglycemic requirement, fasting glucose, Hba1c, anti-lipid requirement, total cholesterol, LDL, HDL, triglycerides, antihypertensive requirement, blood pressure, sleep apnea screening questions, joint pain, panniculitis, hemoglobin, hematocrit, MCV, FE+, Ca+, vitamin B12, folate, prealbumin, and complications. Analysis of these outcomes of surgery will add significantly to the rationale behind bariatric surgery.

**Progress:** This minimal risk protocol remained open to enrollment during FY07, with approximately 50 additional subjects enrolled for a total of 389 subjects enrolled to date. Data collection continues. Currently, clinical outcomes are reviewing the data and an assessment of outcomes related to weight loss and resolution of comorbidities is being performed. There was one death after gastric bypass, due to a known potential complication that and was in no way related to this observational study.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206040	<b>Status:</b> Terminated
<b>Title:</b> Does SDF-1 Production by Atherosclerotic Plaques Correlate with Severity of Carotid Artery Stenosis?		
<b>Principal Investigator:</b> MAJ Daniel R. Cronk, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Garth S. Herbert, MC; COL (Ret) Charles A. Andersen, MD; LTC Benjamin W. Starnes, MC; MAJ Kelly S. Blair, MC; CPT Jason T. Perry, MC		
<b>Start - Completion:</b> 5 Jan 2006 - Dec 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8 Dec 2006

**Study Objective:** To determine whether levels of SDF-1 as measured in atherosclerotic plaques correlates with the severity of disease.

**Technical Approach:** Blood will be drawn from patients scheduled to undergo carotid endarterectomy at the time of surgery or pre-operative evaluation to determine serum SDF-1 levels. In addition, a small section of plaque will be removed from the atherosclerotic plaque excised from twenty patients undergoing carotid endarterectomy at MAMC. The remainder of the plaque will be sent for routine pathological analysis (as is the standard at MAMC). The portion of the specimen used for study purposes will be brought to the Department of Clinical Investigation, where the presence of SDF-1 and possibly other inflammatory mediators will be established using immunohistochemical methods. Segments of radial artery harvested at the time of coronary artery bypass graft will be used as negative controls for immunohistochemical staining. Blood from healthy volunteers will be drawn for control values of serum SDF-1 levels. Regression analysis will be performed to attempt to determine a relationship between the level of SDF-1 in serum/plaques to the degree of carotid artery stenosis.

**Progress:** This protocol was terminated during FY07, due to work refining the staining protocol, as well as changeover in the research residents. No work involving subjects was conducted on this protocol.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203034	<b>Status:</b> Terminated
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**Title:** Impact of Gastric Bypass with Subtotal Gastrectomy on Plasma Ghrelin Profile

**Principal Investigator:** CPT Daniel G. Cuadrado, MC

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** MAJ Philip S. Mullenix, MC; COL Kenneth S. Azarow, MC; MAJ Daniel R. Cronk, MC; CPT Craig S. See, MC; CPT Patrick M. McNutt, MS; COL (Ret) Preston L. Carter, MD; MAJ Alec C. Beekley, MC; CPT Zachary M. Arthurs, MC; MAJ Garth S. Herbert, MC; CPT Katharine E. Wolcott, MC; LTC Matthew J. Martin, MC

**Start - Completion:**

8 May 2003 - Dec 2003

**Funding:**

DCI

**Periodic Review:**

22 Mar 2005

**Study Objective:** To compare the preoperative, immediate postoperative, and 3 month postoperative plasma ghrelin profiles among a cohort of patients undergoing resectional gastric bypass (subtotal gastrectomy combined with roux-en-y bypass). To compare the pre and postoperative plasma leptin and insulin profiles among this patient cohort. To document the change in gross weight, body mass index, and blood pressure among this cohort.

**Technical Approach:** This study will prospectively compare the preoperative and postoperative levels of ghrelin, leptin and insulin in a cohort of patients undergoing resectional gastric bypass. Hormone levels will be obtained one day prior to surgery, two days after surgery, and at three to four months after surgery. Eighteen-hour profiles for each hormone will be generated and area under the curve calculated for comparison. Postoperative complications, amount of weight change, change in body mass index, and change in blood pressure will be recorded and analyzed. Statistical analysis will be done using two-tailed paired Student's t-test where appropriate.

**Progress:** This protocol was administratively terminated by the IRB in March 2007, when several months passed without receiving information from the study staff on a proposed amendment based on recent published data with Ghrelin.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206041	<b>Status:</b> Completed
<b>Title:</b> Breast Abscesses Following Nipple Piercing: A Case Series and Review of the Literature		
<b>Principal Investigator:</b> CPT Daniel G. Cuadrado, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Alec C. Beekley, MC; COL (Ret) Preston L. Carter, MD		
<b>Start - Completion:</b> 5 Jan 2006 - Feb 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8 Dec 2006

**Study Objective:** To review out institutional experience with the treatment of breast abscesses following nipple piercing.

**Technical Approach:** A chart review will be performed and patients separated into 2 groups based upon whether or not they have a pierced nipple on the infected side. Demographic data will be collected and analyzed between the two groups such as age, sex, date of piercing, date of surgery, number of surgical procedures and organism found in the abscess cavity. Data will be analyzed using a t-test for continuous and Chi square for categorical data.

**Progress:** This protocol was reported as completed during FY07. Eight patients with abscesses due to piercing were identified, with a 50% incidence of secondary procedures. The abstract has been submitted to Southwest Surgical Society for consideration for publication.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207049	<b>Status:</b> Ongoing
<b>Title:</b> Is Bariatric Surgery Safe in Patients Over Age 50: A Retrospective Review		
<b>Principal Investigator:</b> CPT Daniel G. Cuadrado, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Kelly E. Lesperance, MC; LTC Matthew J. Martin, MC; COL (Ret) Preston L. Carter, MD		
<b>Start - Completion:</b> 22 Jan 2007 - Mar 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To analyze the perioperative mortality and morbidity, weight loss, and change in comorbid conditions among older patients undergoing gastric bypass.

**Technical Approach:** The prospectively collected MAMC bariatric surgery database will be queried to examine all subjects undergoing bariatric surgery 50 years of age or older. The perioperative mortality and morbidity, weight loss, and change in comorbid conditions among older patients undergoing gastric bypass will be analyzed. Subjects will then be divided into 5th decade vs. 6th decade patients to see if differences exist due to age alone.

**Progress:** This minimal risk protocol was approved by the Expedited Review Committee on 22 January 2007. A progress report has not been requested.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207045	<b>Status:</b> Completed
<b>Title:</b> Bioprosthetic Repair of Severe Duodenal Injuries in sp. <i>Sus scrofa</i>		
<b>Principal Investigator:</b> CPT Matthew J. Eckert, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Matthew J. Martin, MC; MAJ Scott R. Steele, MC; MAJ Alec C. Beekley, MC; CPT Vance Y. Sohn, MC; CPT Jason T. Perry, MC		
<b>Start - Completion:</b> 10 Jan 2007 - Jan 2010	<b>Funding:</b> DCI	<b>Periodic Review:</b> 19 Dec 2007

**Study Objective:** The purpose of this study is to test the efficacy of a porcine dermal bioprosthetic implant in the repair of complex duodenal wall injury. Our hypothesis is that this dermal implant will provide a scaffold for normal healing while maintaining intestinal continuity with subsequent incorporation into native duodenal wall tissue.

**Technical Approach:** Severe duodenal and pancreatic trauma/injury remains one of the most challenging surgical issues. Due to the shared vascular supply of the duodenum and pancreatic head, junction of the common bile duct with the duodenum, and adjacent major vascular structures, injuries in this region force surgeons to find effective, yet regionally preserving, surgical treatment. The pathology of the duodenum requiring surgical care is relatively limited: blunt and penetrating trauma, neoplastic disease, peptic ulcer disease, and adjacent tissue processes remain the most common reasons for duodenal surgery. Traditionally, duodenal wall injuries are repaired primarily whenever possible, with care to avoid narrowing the intestinal lumen, to prevent future stricture or obstruction. Primary repair is usually possible with up to 50% circumferential duodenal wall loss. Unlike other regions of the intestine, resection and subsequent anastomosis are extremely difficult due to the anatomic challenges previously mentioned. Thus, surgeons frequently use alternative surgical strategies such as Graham patch or serosal buttress with or without pyloric exclusion to manage duodenal injury.

Permacol® (Tissue Science Laboratories, Covington, GA) is an acellular collagen bioprosthesis derived from porcine dermal tissue that is currently FDA approved and widely used for rotator cuff repair, soft tissue reconstruction of the abdominal wall and pelvic floor, and reconstructive surgery of the face and head. The collagen scaffold provides a framework for normal wound healing with eventual complete incorporation into normal regenerated host tissue. No studies evaluating the efficacy of Permacol® or other bioprosthetic implants have been published to date involving the repair of duodenal/enteric wall reconstruction. Personal communication with TSL research representatives confirmed prior non-published lab studies exposing Permacol® to acid and bile without evident early product breakdown.

**Progress:** This protocol used eight animals to characterize the effective of Permacol® to treat severe duodenal injuries. The results were very successful with no resulting peritonitis due to duodenal leakage.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207046	<b>Status:</b> Ongoing
<b>Title:</b> Evaluation of the Incidence of Hypovitaminosis and Visual Changes in the Gastric-Bypass Surgery Population		
<b>Principal Investigator:</b> CPT Matthew J. Eckert, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Scott R. Steele, MC; CPT Daniel G. Cuadrado, MC; CPT Jason T. Perry, MC; CPT Vance Y. Sohn, MC		
<b>Start - Completion:</b> 16 Jan 2007 - Apr 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 18 Dec 2007

**Study Objective:** The objectives of this study are to evaluate select vitamin and mineral levels in the MAMC post-bariatric surgery population in order to identify any deficiencies requiring additional supplementation, and to determine the incidence of ocular pathology in this population and identify any potential association between hypovitaminosis A and post-bariatric surgery visual changes.

**Technical Approach:** This is a prospective observational study in which we will attempt to identify the incidence of hypovitaminosis in a post-bariatric surgery population along with any potential association with post-operative vision deterioration related to hypovitaminosis. The study will consist of a mass screening day during which patients will undergo visual acuity testing, blood sampling to determine serum vitamin levels, and a brief focused history and physical exam pertinent to their bariatric surgical procedure. Patients will receive a detailed questionnaire concerning post-operative recovery, dietary habit, and any vision deterioration prior to the screening day. Those patients with concerning survey answers, lab results, or visual screening results will receive appropriate follow-up appointments for further evaluation. The primary endpoints of interest will be identification of vision complaints/screening abnormalities and select serum vitamin and mineral deficiencies, with secondary endpoints of changes/resolution of pre-operatively identified weight related comorbidities, change in BMI, and changes in use of nutritional supplementation. Primary endpoints will be analyzed using a one sample binomial test and secondary endpoints will be evaluated with a paired t-test and chi square. Univariate and multivariate analysis will be conducted to determine factors dependently and independently associated with the primary endpoints of interest.

**Progress:** This minimal risk protocol was approved by the Expedited Review Committee on 16 January 2007. Investigators screened 73 patients with a surgical history of open or laparoscopic gastric bypass surgery for nutritional deficiencies and ocular symptoms potentially related to Vitamin A deficiency during the spring of 2007. Of this group, nine patients were identified as having low vitamin A levels. Supplemental nutritional guidance from Clinical Nutrition was provided to these nine patients. In addition, the Ophthalmology Clinic screened all patients for potential ocular manifestations of low vitamin A levels. Some ocular examinations remain ongoing. Patient lab data is currently being summarized and correlated from the survey related to nutritional deficiencies after weight loss surgery. All patients with lab abnormalities will have had appropriate referral for additional examination as required.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 201020	<b>Status:</b> Ongoing
<b>Title:</b> Learning Curves for Airway Assessment and Endotracheal Intubation - Cumulative Sum Analysis		
<b>Principal Investigator:</b> MAJ Garth S. Herbert, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kenneth S. Azarow, MC; COL Joseph P. Miller, MC; LTC James A. Sebesta, MC; CPT James C. Nunley, MC; LTC Gregory P. Fitzharris, MC; CPT Craig S. See, MC; MAJ Jennifer E. Jorgensen, MC; LTC Ronald J. Place, MC; CPT Jeffrey S Kunz, MC; LTC Alan L. Beitler, MC; CPT Amy L. Young, DO		
<b>Start - Completion:</b> 28 Nov 2000 - Jul 2002	<b>Funding:</b> DCI	<b>Periodic Review:</b> 5 Dec 2007

**Study Objective:** (1) To evaluate individual and institutional learning curves for airway assessment by analyzing diagnostic accuracy as a function of experience for a group of surgical interns performing a 4-week rotation on the anesthesia service, (2) To develop individual and institutional learning curves for the skill of endotracheal intubation as a function of experience for a group of surgical interns performing a 4-week rotation on the anesthesia service, and (3) To evaluate a model (Cumulative sum analysis) for assessing the technical proficiency of surgical interns in the skills of airway assessment and endotracheal intubation.

**Technical Approach:** Surgical interns will receive standardized training on airway anatomy and assessment coupled with a practical session on intubation in ATLS models. These house officers will then perform airway assessments and endotracheal intubations on surgical patients who are 18 years or older, ASA class I or II, and who do not require rapid sequence intubation. Each attempt will be supervised and scored by a staff anesthesiologist or CRNA using a standardized data sheet. A successful assessment will be one where the airway classification matches the supervising staff's determination. A successful intubation will be insertion of an endotracheal tube within 30 seconds of laryngoscopy initiation, documented by end tidal CO<sub>2</sub>. If an attempt is unsuccessful, the process may be repeated. Each consecutive attempt will be recorded separately. A data sheet will be filled out and a new score assigned for each attempt, even when there are multiple attempts on a single patient. Supervising staff will determine if and when they need to step in and intubate the patients themselves.

Data sheets will be turned in to the principal investigator, who will calculate CUSUM values and plot learning curves. Data will be monitored during the rotation. At the completion of the 4-week experience, these results will be shared with the interns and staff. After an entire class of interns has completed the rotation, the results will be submitted for publication and presentation.

**Progress:** Due to deployments and staffing changes in the Simulations Center, no enrollment occurred in this study during FY07. Investigators will attempt to enroll the current group of interns in to the study to be able to determine the minimum number of colonoscopies required to become proficient.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205063	<b>Status:</b> Completed
<b>Title:</b> The Impact of Nodal Micrometastases on Survival of Women with Breast Cancer		
<b>Principal Investigator:</b> MAJ Garth S. Herbert, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 6 Apr 2005 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 21 Mar 2006

**Study Objective:** To establish whether the presence of nodal micrometastases in breast cancer is predictive of a worse outcome.

**Technical Approach:** This study is a retrospective review of all women diagnosed with breast cancer at MAMC between 1996 and 2003. Survival and disease-free survival will be compared in patients with benign lymph nodes and those with microscopic evidence of metastasis (tumor foci < 2mm and diagnosed by hematoxylin and eosin stain or immunohistochemistry). Other potential investigations include (but are not limited to) analysis of the sensitivity of touch prep for analysis of sentinel lymph nodes at MAMC, and survival in patients with metastasis to the sentinel lymph node who do or do not have an axillary dissection.

**Progress:** Over 400 patients records were reviewed, but only 16 were identified with isolated tumor cells detected in lymph nodes. Patient and tumor characteristics, as well as recurrence and survival rates were compared to women with node negative disease. Investigators did not detect a difference in recurrence or survival rates in patients with isolated tumor cells. Results will be presented at the North Pacific Surgical Association, and a manuscript is being forwarded to DCI. Awaiting publication of the manuscript in the American Journal of Surgery.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205125	<b>Status:</b> Terminated
<b>Title:</b> Prospective, Randomized, Placebo-Controlled Trial of Tegaserod for Treatment of Delayed Gastric Emptying after Pancreaticoduodenectomy		
<b>Principal Investigator:</b> MAJ Garth S. Herbert, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Tommy A. Brown, MC; COL Kenneth S. Azarow, MC		
<b>Start - Completion:</b> 9 Jan 2006 - Sep 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 28 Aug 2006

**Study Objective:** To determine the efficacy of Tegaserod for relief of delayed gastric emptying after pancreaticoduodenectomy.

**Technical Approach:** 70 TRICARE beneficiaries scheduled to undergo pancreaticoduodenectomy will be asked to enroll. Subjects will be randomized to receive either placebo or Tegaserod 6 mg, orally, twice a day once oral intake is allowed following pancreaticoduodenectomy. Subjects will be monitored for evidence of delayed gastric emptying and return of bowel function (flatus, bowel movements). The time between surgery and discharge will also be recorded. The percentage of patients in each group with delayed gastric emptying will be compared using the Mann-Whitney test to determine whether Tegaserod provided any benefit in reducing the incidence of DGE.

**Progress:** This protocol was terminated when the study medication, Tegaserod (Zelnorm), was removed from the market by the manufacturer, since it appears to increase the risk of both myocardial infarction and stroke. Three patients were enrolled, one of whom died before receiving the study medication. The two patients who did receive the study medication both received placebo, so there were no adverse events related to Tegaserod.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205126	<b>Status:</b> Terminated
<b>Title:</b> Prospective, Randomized, Placebo-Controlled Trial of Tegaserod for Treatment of Post-Operative Ileus Following Partial Colectomy		
<b>Principal Investigator:</b> MAJ Garth S. Herbert, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Tommy A. Brown, MC; COL Kenneth S. Azarow, MC; CPT Katharine E. Wolcott, MC		
<b>Start - Completion:</b> 9 Jan 2006 - Sep 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 26 Sep 2006

**Study Objective:** To determine the efficacy of Tegaserod for amelioration of post-operative ileus following partial colectomy

**Technical Approach:** 60 TRICARE beneficiaries scheduled to undergo partial colectomy will be asked to enroll. Subjects will be randomized to receive either placebo or Tegaserod 6 mg orally, twice a day beginning the day following surgery. Data will be collected on length of hospital stay, time between surgery and first flatus, first bowel movement, and the time until tolerating a regular diet. The average hospital stay will be compared between the control and study groups using the Student's t-test.

**Progress:** This protocol was terminated when the study medication, Tegaserod (Zelnorm), was removed from the market by the manufacturer, since it appears to increase the risk of both myocardial infarction and stroke. Fifteen patients enrolled, nine of whom received Tegaserod. The patient's records were reviewed from the time of surgery to the present and none have suffered from a myocardial infarction or stroke. All other adverse events have been previously reported to the IRB. The limited number of patients accrued during the study, as well as a lack of difference between length of hospital stay between the study and control groups prevent meaningful conclusions from being drawn from our data. (An analysis performed with the data obtained thus far revealed no statistically significant difference between hospital stay or return of bowel function with the use of tegaserod as compared to placebo). For this reason, prefer to terminate the study rather than close it prematurely.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206010	<b>Status:</b> Terminated
<b>Title:</b> Does Control of Inflammation Prior to Intervention for Carotid Artery Disease or Lower Extremity Peripheral Arterial Disease Affect Outcome?		
<b>Principal Investigator:</b> MAJ Garth S. Herbert, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD; LTC Benjamin W. Starnes, MC		
<b>Start - Completion:</b> 6 Feb 2006 - Jul 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 19 Oct 2006

**Study Objective:** This study will determine the effect that a 30-day course of aspirin and statins have on inflammation, as measured by CRP levels and determine whether peri-operative management of inflammation affects outcome (specifically re-stenosis / myointimal hyperplasia) following intervention for Carotid Artery Stenosis or Peripheral Arterial Disease.

**Technical Approach:** Participants in this study will include up to 200 volunteers who require intervention for CAS, in addition to 120 who require intervention for lower extremity PAD. Patients will be randomized to either intervention alone (surgery or angioplasty/stenting) accompanied by moderate statin therapy (standard of care for patients with atherosclerotic disease), or a 90-day peri-operative course of atorvastatin and aspirin directed at reducing the degree of systemic inflammation (to include 30 days pre-operatively and 60 days post-operatively). CRP levels will be measured in each group at baseline, pre-operatively, and during follow up visits. Subjects will undergo surgery for carotid artery stenosis, or intervention for lower extremity PAD. Complications, to include myocardial infarction, stroke, death, and in particular, re-stenosis will be measured in each group. The number of complications in each group (those simply undergoing surgery, and those who have surgery accompanied by a 90-day regimen of anti-inflammatory medications) will be compared to determine whether control of inflammation has an impact on outcome of intervention for carotid artery stenosis or peripheral arterial disease.

**Progress:** This protocol was reported as terminated during FY07, with no subjects enrolled. Work on other protocols has superseded this research. Of patients who might qualify for the study, many were already on high doses of statins (exclusion criteria), and others could not wait thirty days prior to the required intervention, which was necessary for the anti-inflammatory therapy of statin/ASA.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206026	<b>Status:</b> Completed
<b>Title:</b> Determination of Telomerase Activity in Atypical Ductal Hyperplasia of the Breast		
<b>Principal Investigator:</b> MAJ Garth S. Herbert, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Vance Y. Sohn, MC; COL Kenneth S. Azarow, MC; MAJ Anne L. Champeaux, MC; CPT Matthew J. Eckert, MC; CPT Michael J. Mulcahy, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 14 Dec 2005 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 20 Mar 2007

**Study Objective:** The objective of this study is to determine the presence and prognostic significance of telomerase activity in breast atypical ductal hyperplasia and whether telomerase activity in Stage I breast carcinomas is predictive of the incidence of recurrence.

**Technical Approach:** A review of Breast pathway charts will be completed to identify 20 patients with a diagnosis of atypical ductal hyperplasia on core biopsy who went on to open surgical biopsy. Ten of these patients will have ductal carcinoma in situ (DCIS) or invasive cancer identified at open surgical biopsy and ten will have benign pathology. In addition, 100 patients will be identified who have been diagnosed with Stage I breast cancer, 50 of whom remain disease free, and 50 in whom disease recurred. Data will be coded and immunohistochemistry performed on the paraffin slides of these tissues. A staff pathologist will evaluate the degree of hTERT staining, and will confirm the diagnosis of ADH. The pathologic diagnosis on open surgical biopsy will be compared and correlations made (if any) between intensity of staining and the presence/absence of cancer on open surgical biopsy. For those patients with Stage I breast cancer, comparisons will be made between the degree of hTERT staining in the group that remains disease free as compared to those in whom disease recurred.

**Progress:** This protocol was reported as completed during FY07. Results: Core biopsy specimens stained strongly with the hTERT antibody in 7 (70%) specimens with ADH on open biopsy and 6 (86%) with underlying cancer. The difference was not statistically significant ( $P = 0.43$ ). The manuscript was published in the American Journal of Surgery vol 193 (2007); pp 547–550.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206027	<b>Status:</b> Ongoing
<b>Title:</b> Prognostic Significance of Telomerase Activity in T1 and T2 Rectal Adenocarcinoma for Patients Undergoing Transanal Excision		
<b>Principal Investigator:</b> MAJ Garth S. Herbert, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Tommy A. Brown, MC; COL Kenneth S. Azarow, MC		
<b>Start - Completion:</b> 14 Dec 2005 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 26 Nov 2007

**Study Objective:** To determine the presence and prognostic significance of telomerase activity in rectal adenocarcinoma for patients who undergo trans-anal excision of these lesions.

**Technical Approach:** Madigan Army Medical Center operative charts will be reviewed to identify 20 patients with a diagnosis of rectal adenocarcinoma who have undergone transanal excision. This data will be coded and immunohistochemistry performed on the paraffin slides of these tissues. Clinical outcome data will be compared in an attempt to make correlations between the degree of telomerase activity and pathologic stage, as well as with the incidence of recurrence. Telomerase activity may prove to be prognostic indicator of which patients should undergo more aggressive surgery in the management of rectal adenocarcinoma.

**Progress:** This bench protocol remains ongoing with fourteen patients identified who previously underwent transanal excision of rectal cancer. Testing was performed on old surgical specimens; however there are insufficient numbers to determine whether positive staining for telomerase is predictive of whether tumors will recur. In order to have sufficient power to determine whether telomerase staining is a worthwhile procedure in evaluating rectal cancer, investigators have requested pathology slides from Fox Chase Cancer Center, and have obtained their IRB's approval. Once slides have arrived, the protocol will continue with final data analysis.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207037	<b>Status:</b> Ongoing
<b>Title:</b> The Association of Ethnicity with Presentation and Mortality in Colorectal Cancer		
<b>Principal Investigator:</b> CPT Monique O. Hopkinson, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Scott R. Steele, MC		
<b>Start - Completion:</b> 9 Jan 2007 - Dec 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 12 Dec 2007

**Study Objective:** This study is designed to compare the stage, grade, and survival between colorectal cancer patients of different ethnicities treated at tertiary military medical facilities.

**Technical Approach:** This study is a retrospective chart/tumor registry review designed to compare the age, grade, stage, treatment and outcome data amongst colorectal cancer patients of varying ethnicities over a ten year period.

**Progress:** This minimal risk protocol was approved by the Expedited Review Committee 9 January 2007. Investigators continue to analyze the 475 records from the tumor registry. Some conclusions have been made regarding race and treatment outcomes, but investigators continue to look at specific treatments and access to care.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206043	<b>Status:</b> Completed
<b>Title:</b> Colorectal Complications of External Beam Radiation vs. Brachytherapy for Prostate Cancer		
<b>Principal Investigator:</b> CPT Randy J. Kjorstad, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Matthew J. Martin, MC; MAJ Philip S. Mullenix, MC; COL John B. Halligan, MC; MAJ Scott R. Steele, MC; CPT Richard N. Lesperance, MC		
<b>Start - Completion:</b> 9 Jan 2006 - Feb 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 16 Jan 2007

**Study Objective:** The objective is to determine the prevalence and significance of colorectal complications (i.e. bleeding, ulceration, proctitis, incontinence) following external beam radiation therapy versus brachytherapy for prostate cancer.

**Technical Approach:** A chart review of all cases of each modality will be performed and colon and rectal complications compared as well as functional outcome for each approach. Records in the radiation oncology clinic will be used to generate the patient names for each of the two methods. Data will be collected and organized on an excel spreadsheet for analysis.

**Progress:** This protocol was reported as completed during FY07. A paper has been accepted for presentation at the 2007 North Pacific Surgical Association meeting in British Columbia, and is being reviewed for publication in the American Journal of Surgery. Results: 183 patients underwent EBRT and 50 BT with a mean follow-up of 39 months. BT was associated with significantly less acute (6% vs. 43.5%) and late toxicities (2% vs. 21.8%; both  $p < 0.001$ ). Among patients receiving EBRT, acute grade 3 toxicity was experienced by 1 (0.5%) patient, and grade 2 toxicity by 79 (43%). Increased stool frequency was the most common manifestation (62%), followed by rectal pain and urgency (30%) and rectal bleeding (21%). Late toxicity included 34 (18.6%) patients with grade 2 (bleeding (68%), frequent stools (26%), pain and urgency (18%)), and 5 patients (2.7%) with grade 3 toxicity (bleeding requiring multiple cautery procedures (3), small bowel obstruction requiring surgery (1), anal stenosis requiring repeat dilations (1)). BT was relatively well-tolerated, with only 3 patients (6%) experiencing grade 2 acute toxicity symptoms of pain and urgency. One BT patient suffered late grade 2 toxicity of bleeding requiring intervention. One patient developed rectal cancer 20 years after EBRT. Conclusions: Despite its relative safety, radiation therapy frequently requires medical therapy for complications, as well as endoscopic or surgical intervention for more severe complications. Overall BT has a significantly lower incidence of acute and late toxicities than EBRT.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207058	<b>Status:</b> Ongoing
<b>Title:</b> Prevalence and Outcomes of Headache Disorders in Obese Patients Undergoing Gastric Bypass Surgery for Weight Loss		
<b>Principal Investigator:</b> CPT Matthew P. Kozminski, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Jay C. Erickson, MC		
<b>Start - Completion:</b> 23 Jan 2007 - Nov 2009	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objectives of this study are to determine (1) the prevalence of primary headache disorders among a morbidly obese population seeking gastric bypass for weight loss, and (2) if headache symptoms improve following weight loss secondary to a resectable gastric bypass (RGB) or laparoscopic gastric bypass (LGB).

**Technical Approach:** Two hundred and forty (240) obese individuals seeking weight reduction by RGB or LGB at the MAMC General Surgery Clinic will be asked to voluntarily complete a standardized headache questionnaire, based on IHS criteria for primary headache disorders and the MIDAS (Migraine Disability Assessment Scale), during their preoperative education and planning sessions. Responses will calculate the prevalence, frequency, severity, and duration of headaches among a morbidly obese population. All subjects who screen positive for a headache disorder will be contacted by the research coordinator by phone within two weeks prior to surgery, six months after surgery in order to complete a follow up headache questionnaire. The change in headache severity, frequency, and disability will be correlated with weight loss.

**Progress:** This minimal risk protocol received initial approval by the Expedited Review Committee on 23 January 2007. No changes to the protocol or progress reports have been submitted.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204001	<b>Status:</b> Ongoing
<b>Title:</b> Does Intestinal Fatty Acid Binding Protein Predict Strangulation in Mechanical Small Bowel Obstruction?		
<b>Principal Investigator:</b> CPT Ryan K. Lehmann, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Randy J. Kjorstad, MC; CPT Daniel G. Cuadrado, MC; COL Kenneth S. Azarow, MC; CPT Patrick M. McNutt, MS; MAJ Daniel R. Cronk, MC; CPT Troy P. Houseworth, MC		
<b>Start - Completion:</b> 24 Oct 2003 - Dec 2003	<b>Funding:</b> DCI	<b>Periodic Review:</b> 2 Oct 2007

**Study Objective:** To determine if intestinal fatty acid binding protein (I-FABP) levels are elevated in patients with strangulated mechanical small bowel obstruction.

**Technical Approach:** This is a prospective, observational, pilot study investigating the utility of intestinal fatty acid binding protein (I-FABP) for detecting strangulated mechanical small bowel obstruction. Thirty consecutive patients presenting to the general surgery service with mechanical bowel obstructions will be enrolled and have plasma and urine I-FABP levels analyzed at the time of admission, time of operation, and 24 hours after operation (should they require operative intervention). Using multivariate analysis, levels of plasma and urine I-FABP will be compared between those patients without ischemia and those with ischemia upon operative exploration to determine if I-FABP is a potentially useful marker for the prospective identification of strangulated small bowel obstruction.

**Progress:** This minimal risk protocol remains open to enrollment with a total of 28 subjects thus far, none during FY07. A change in the role of principal investigator from MAJ Cronk to CPT Lehmann was submitted and approved.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206115	<b>Status:</b> Ongoing
<b>Title:</b> Hypoxemic Reperfusion Following Lower Torso Ischemia in sp. Sus scrofa		
<b>Principal Investigator:</b> CPT Ryan K. Lehmann, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Matthew J. Eckert, MC; LTC Matthew J. Martin, MC; CPT Vance Y. Sohn, MC; CPT Jason T. Perry, MC		
<b>Start - Completion:</b> 23 Aug 2006 - Aug 2009	<b>Funding:</b> DCI	<b>Periodic Review:</b> 11 Jul 2007

**Study Objective:** Hypothesis is that hypoxemic reperfusion (PaO<sub>2</sub> 30-35mmHg) compared with normoxemic reperfusion (PaO<sub>2</sub> 100mmHg) following lower torso ischemia induced by supra-celiac aortic cross-clamping results in improved hemodynamic stability and pulmonary gas-exchange, decreased vasoactive medication requirements, decreased reperfusion injury induced histopathologic changes in multiple organ systems, and less evidence of reactive oxygen species activity. Additionally, hypothesize that the hypoxemic reperfusion strategy will limit the hind-leg compartment pressure compared to normoxemic reperfusion.

**Technical Approach:** V.1. Experimental Design and General Procedures: This experiment will be conducted in a multi-phase format, beginning with a pilot study to determine the feasibility of our model. This general protocol will cover the basics of the overall experimental goal, but subsequent amendments will detail successive phases as dictated by success of the pilot study and refinement of various techniques.

Phase I (Pilot Study): The pilot study will utilize a total of four pigs. After establishment of general anesthesia, arterial vascular access will be obtained for continuous pressure monitoring at the common carotid or femoral artery using a cut-down approach and Seldinger cannulation technique. Hind leg compartment pressure will be monitored continuously using an arterial catheter placed percutaneously into a hind-leg musculo-fascial compartment. Venous access via the jugular vein will be obtained for intra-venous fluid and medication administration. An additional lower extremity vein (likely femoral vein) will be accessed for sampling of the ischemic region of the body. Ventilatory parameters will be adjusted to maintain baseline blood gas parameters during the access and ischemia portions of the experiment (PaO<sub>2</sub> 70-90mmHg, PCO<sub>2</sub> 40-50, pH 7.4-7.55 and saturations of 92-98%) After baseline stabilization and laboratory analysis (blood gas, lactate, chem.-7 panel), a midline laparotomy will be performed with cross-clamping of the supra-celiac aorta for 60 minutes. A supra-pubic bladder catheter will be placed to allow for measurement of urine production during the ischemic and reperfusion phases. Prior to the end of 60 minutes of ischemia repeat lab samples will be performed. During the last 10 minutes of ischemia ventilatory management will alter the PaO<sub>2</sub> to a goal of 30-35mmHg by decreasing the fraction of inspired O<sub>2</sub> (FiO<sub>2</sub>), for the hypoxemic reperfusion group (HR). The normoxemic reperfusion group (NR) will enter the reperfusion phase with a goal PaO<sub>2</sub> of 95-105mmHg. Once these ventilatory parameters are met, the cross-clamp will be released, with serial hemodynamic measurements every 15 minutes during the 120 minute reperfusion phase with repeat lab sampling every 30 minutes and continuous compartment pressure monitoring. During the ischemic and reperfusion phase lactated ringer's fluids and epinephrine will be used as needed to maintain the baseline MAP (Douzinias et al. Crit Care Med 2003;31:2183 found that 50ug/min i.v. epinephrine just prior to cross-clamp release and as need thereafter prevented immediate cardiac arrest). The total intra-venous fluid and pressor medication requirements will be recorded for comparison. The protocol of ventilatory management for the HR group during the reperfusion phase is as follows: 10 minutes of a goal PaO<sub>2</sub> of 30-35mmHg, followed by gradual increase of the FiO<sub>2</sub> to achieve a goal PaO<sub>2</sub> of 50mmHg at 60 minutes reperfusion and finally 100mmHg at 120 minutes of reperfusion. Following reperfusion completion and final lab/hemodynamic value

recording, the animals will be euthanized.

V.1.2. Phase II: Following confirmation of our experimental model from Phase I, we plan to conduct a full trial of hypoxemic vs. normoxemic reperfusion with additional biochemical and pathologic analysis evaluating the activity and effects of reactive oxygen species. The ischemia-reperfusion model will be identical unless found to require modification during the pilot and appropriately addressed in an addendum. Phase II will include post-mortem tissue sampling of lung, liver, kidney and brain for histopathologic evidence of ischemia/inflammatory changes. This will be conducted by two pathologists unaware of the animal's reperfusion strategy, with organ injury graded by a predetermined scale. Inter-observer variability will be calculated. Additional biochemical analysis during Phase II will include measurement of free radical activity and effects. This will be conducted using venous whole blood samples with commercially available kits for oxygen free radical activity and superoxide dismutase (Trevigen, Gaithersburg, MD) assays, along with determination of xanthine oxidase activity (Invitrogen, USA). The detrimental effects of lipid peroxidation by free radicals will be determined with malonaldehyde (MDA) and hydroxyalkenal assays of whole blood samples (Calbiochem, San Diego, CA). We tentatively plan to use a total of 20 pigs during Phase II, ten in each group. We reserve the right to change the commercial assay kits if a cheaper, equivalent product is found in order to reduce the cost of this experiment. Such changes would be detailed in subsequent amendments as needed.

V.1.3. Phase III: Phase III is a potential further experimental trial evaluating the beneficial effects of known free radical scavengers (mannitol, allopurinol, superoxide dismutase) in concert with a hypoxemic reperfusion strategy for improved control/modulation of the reactive oxygen species contribution to reperfusion injury. This Phase will be addressed in a future amendment pending successful completion of Phase I/II and statistical analysis to determine the number of animals required to show a significant difference between treatment groups.

**Progress:** This protocol used seven animal models to characterize the effects of lower torso ischemia in the pig. The model will be further develop in FY 08 to study different reperfusion techniques for use in combat casualties.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207115	<b>Status:</b> Ongoing
<b>Title:</b> Madigan Army Medical Center Trauma System Triage Criteria Study		
<b>Principal Investigator:</b> CPT Ryan K. Lehmann, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Matthew J. Martin, MC; CPT Matthew J. Eckert, MC; CPT Zachary M. Arthurs, MC		
<b>Start - Completion:</b> 6 Aug 2007 - 07/08	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this protocol is to prospectively compare the current MAMC Trauma Triage criteria with a set of alternative criteria developed during a previous retrospective study.

**Technical Approach:** This study is a prospective comparison of current MAMC/Pierce County Pre-hospital Trauma Triage criteria with a set of alternative triage criteria previously identified in retrospective analysis as independent predictors of requirement for urgent intervention. The data will be collected from the current routine practice of the Trauma Registrar and MAMC Trauma Database, as well as data on "mis-triage" collected by the investigators. Conclusions from this study will potentially help to revise/devise an accurate, safe and efficient trauma triage criteria system that identifies injured patients likely in need of surgical support/care, thus limiting over-triage and poor resource management.

**Progress:** This minimal risk protocol received final approval by the Expedited Review Committee, effective 6 August 2007.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207117	<b>Status:</b> Ongoing
<b>Title:</b> Efficacy of Topical Hemostatic Dressings Following Subclavian Artery Injury in Sus Scrofa		
<b>Principal Investigator:</b> CPT Ryan K. Lehmann, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Matthew J. Martin, MC; MAJ Alec C. Beekley, MC; CPT Matthew J. Eckert, MC; CPT Vance Y. Sohn, MC; CPT Jason T. Perry, MC; LTC Robert M. Rush, MC; LTC James A. Sebesta, MC		
<b>Start - Completion:</b> 15 Aug 2007 - 8/14/2010	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective of this study is to see if the Chitoflex™ dressing provides improved hemostatic efficacy in a porcine deep penetrating vascular injury model, when compared to Quickclot® topical hemostatic agent. The secondary objective will be to maximize animal usage through the subsequent training of general surgery and urology residents in trauma/emergent surgical procedures.

**Technical Approach:** This experiment will consist of three hemostatic testing arms; animals will be randomized immediately following injury to one of three groups: one utilizing temperature controlled Quickclot® zeolite granular powder (Quickclot ACS+® (n=8)), the second using the new HemCon Chitoflex™ dressing (n=8), and the third using a standard gauze Kerlex roll to serve as control (n= up to 8). Since several previous models testing various hemostatic agents have used gauze as the control dressing with almost uniform failure, we intend to start with four animals in the gauze group. If three or more of the gauze/control animals fail, additional testing of the gauze group will be discontinued, thus potentially reducing the total animal numbers. The animal injury model will consist of a standardized hemi-transection of the subclavian artery, thus creating a potentially lethal hemorrhage from a high pressure vascular system.

Recordable data variables will include: hemodynamic parameters (blood pressure, mean arterial pressure, heart rate), total blood loss, survival, lab values (hematocrit, lactate, base deficit), dressing failure, thoracic girth, Doppler flow through brachial artery and thromboelastometry parameters. T-test for independent samples will be used to compare continuous variables and Chi-square analysis of categorical mortality and dressing failure data. Interim analysis will be conducted with help from the DCI statistician after four animals from each group have been studied, to confirm sample size needed to find statistical significance.

**Progress:** This protocol received initial approval 15 August 2007. No work was conducted on this study during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205080	<b>Status:</b> Ongoing
<b>Title:</b> Stem cell engraftment in the lipopolysaccharide mouse (Mus musculus) model of acute inflammatory injury		
<b>Principal Investigator:</b> CPT Kelly E. Lesperance, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Matthew J. Eckert, MC; MAJ Daniel R. Cronk, MC; CPT Daniel G. Cuadrado, MC; CPT Kerry L. O'Brien, MC; COL Kenneth S. Azarow, MC; MAJ Garth S. Herbert, MC		
<b>Start - Completion:</b> 11 May 2005 - May 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 30 May 2007

**Study Objective:** To investigate the most efficient conditions under which to administer stem cells to mice following experimentally induced inflammatory injuries.

**Technical Approach:** This study will be carried out in four phases. The first phase will be a pilot study to develop the LPS injury model in this laboratory, to further characterize a number of molecules that play a role in stem cell movement but have not been studied in LPS injury, and to accurately define the optimal timing for administration of cellular therapies to enhance their eventual engraftment in the target tissue. LPS injuries in the lung and skeletal muscle will be utilized. The first phase will also involve in vitro studies of the cultured bone marrow from mice euthanized during this first phase. The in vitro studies will allow us to evaluate cell culture treatments that may enhance the administered stem cells. To date, the pulmonary LPS injury has been demonstrated reproducibly in our lab from our previous studies. To complete phase 1 similar LPS challenges in skeletal muscle will be performed. This will be accomplished by intramuscular injection of LPS with animal sacrifice at 0, 6, 12, 24, 48 and 72 hours. The muscle samples will be analyzed by histology, immunohistochemistry and ELISA. The second phase of this study will involve using various pro and anti-inflammatory cytokines to modulate the local immune response following LPS induced injury. To date in our lab we have demonstrated that stromal derived growth factor 1 (SDF-1) is modulated following LPS induced lung injury. This cytokine has been previously demonstrated to be essential for stem cell engraftment following bone marrow transplant. In order to further characterize the role of SDF-1 in inflammatory injury, we will measure tissue levels following LPS challenge. Furthermore, through the use of cytokine delivery systems we will characterize the effect of dyschronic administration of SDF-1 on the inflammatory cascade. Using 100 micron heparin sulfate bonded acrylic beads injected into the subcutaneous tissue (along with bupivacaine to reduce pain) we will examine the cellular response both in the presence as well as in the absence of LPS. The third phase of this study will involve transplantation of bone marrow into LPS injured mice and evaluation of engraftment into target tissues at various time points. For this phase of the protocol, LPS will be administered through either direct injection (i.e. intratracheally, intraperitoneally) or through a subcutaneous delivery system in the thigh (heparin sulfate impregnated beads). The fourth phase of this study will combine information from the first three phases and determine if the putatively successful maneuvers evaluated in phase one actually enhance engraftment of transplanted bone marrow cells.

**Progress:** During FY07, this protocol continued to characterize the inflammatory effects of LPS in various tissues. Ultimately this protocol will be used to determine treatments that will minimize the inflammatory response of LPS in tissues such as lung, muscle and other viscera.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206004	<b>Status:</b> Ongoing
<b>Title:</b> The Evaluation of Telomerase Inhibition in a Colorectal Metastasis Model Using Nude Mice ( <i>Mus musculus</i> )		
<b>Principal Investigator:</b> CPT Kelly E. Lesperance, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Vance Y. Sohn, MC; LTC Tommy A. Brown, MC; COL Kenneth S. Azarow, MC; CPT Jason T. Perry, MC; MAJ Garth S. Herbert, MC		
<b>Start - Completion:</b> 8 Nov 2005 - Oct 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 12 Sep 2007

**Study Objective:** This study will test imatinib mesylate in vivo to determine its efficacy in limiting metastatic spread of human colon cancer in nude mice.

#### Technical Approach:

##### Experiment 1

A pilot study will be conducted to validate the method of delivery of tumor cells. Mice will be anesthetized under standard policy as per the MAMC veterinarian. 26 mice will be used, 13 in each group. A mini-laparotomy will be performed and the spleen mobilized. Approximately 4 million colon cancer cells suspended in saline vs. saline alone will be injected into the subcapsular space of the spleen using a 26 gauge needle. After 10 minutes, the splenic vessels will be ligated, and the spleen removed. The abdominal incision will then be closed using simple interrupted sutures of 4.0 Vicryl. The animals will then be returned to their cages, which will be maintained at 90oF until animals have recovered fully from anesthesia. They will be allowed food and water ad lib. All mice will be observed for evidence of study endpoints. All surviving mice will be sacrificed at 60 days following surgery. The liver will be removed, and weighed in order to quantify the extent of metastatic spread. Data from mice who had saline alone injected into the spleen will be used establish a baseline liver weight. The percentage of mice surviving, as well as the length of time required for appreciable tumor growth may dictate modification of these factors in subsequent experiments.

##### Experiment 2

After verifying that the above model of tumor metastasis functions effectively, we will begin the second arm of the study. Mice will undergo the same procedure as detailed above. We intend on using 13 mice per group, although survival results and tumor size in Experiment 2 may require modifications. One half of the mice will then be administered imatinib mesylate (10mg/kg/day) orally (gavage), while mice in the control group will receive saline gavage. Again, the animals will be allowed food and water ad lib. All mice will be observed daily, watching for study endpoints as detailed in V.4.5. All surviving mice will be sacrificed at 60 days following surgery. The liver will be removed, and weighed in order to quantify the extent of metastatic spread. The mass of the liver will be compared between the two groups to quantify the ability of imatinib mesylate to inhibit metastatic spread of colon cancer. In addition, portions of the liver will also be frozen for subsequent quantification of telomerase activity.

##### Experiment 3

Additional experiments using the model established above will be conducted using other telomerase inhibitors, as compared to imatinib mesylate, or in conjunction with established anti-neoplastic agents with efficacy against colon cancer, such as 5-fluorouracil, irinotecan, capecitabine and bevacizumab. Again, based on preliminary power analysis, 13 animals will be required per group (with approximately 8 groups to include a control group, an imatinib only

group, and multiple groups that receive other antineoplastic agents with or without imatinib).

**Progress:** The plan was for a multi-armed procedure using mice. During the first pilot study, a power analysis was performed after completion as described in the original protocol in which the numbers required to proceed was greater than 40,000 mice. Therefore, a repeat pilot was performed; however, this too was unsuccessful. Investigators are currently reviewing the literature to determine the technical aspects to continue with this protocol. No work was conducted on this protocol during FY07, but is expected to be initiated during FY08.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207103	<b>Status:</b> Ongoing
<b>Title:</b> The Yield of Postoperative Fever Workup in General Surgical Patients		
<b>Principal Investigator:</b> CPT Richard N. Lesperance, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Matthew J. Martin, MC; MAJ Daniel R. Cronk, MC; CPT Ryan K. Lehmann, MC; CPT Kelly E. Lesperance, MC		
<b>Start - Completion:</b> 12 Jun 2007 - Jul 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this protocol is to determine the details of evaluations performed in post-operative patients with fevers, and the yield of those evaluations in identifying the etiology of the fever.

**Technical Approach:** All adult patients will be identified who underwent in-patient surgical procedures by the Department of Surgery, General Surgery Service over the course of a calendar year. Of those patients that experienced a fever of greater than 100.4 in the immediate 72 hours post-op, diagnostic evaluations formed as part of a "fever workup" by the responsible house officer will be recorded and whether the results of those evaluations changed the management of the patient. Investigators hypothesize that, in accordance with the small number or previously published studies, the overwhelming majority of fever workups do not change the management of the patient and fail to identify any treatable source of fever.

**Progress:** This minimal risk protocol received final approval by the Expedited Review Committee, effective 12 June 2007. An amendment adding CPT Kelly Lesperance, MC, Resident, General Surgery Service, as an Associate Investigator was approved 20 August 2007.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206079	<b>Status:</b> Ongoing
<b>Title:</b> The Utility and Impact of Standard Trauma Triage Criteria in the Elderly		
<b>Principal Investigator:</b> LTC Matthew J. Martin, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Ryan K. Lehmann, MC; CPT Matthew J. Eckert, MC		
<b>Start - Completion:</b> 13 Apr 2006 - Oct 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 3 Apr 2007

**Study Objective:** To analyze and compare the trauma triage criteria and implementation as well as outcomes among elderly (age>65) trauma victims in the State of Washington.

**Technical Approach:** This is a retrospective study utilizing pooled data collected from several different hospitals in the State of Washington over a four year period and placed on a database. Variables pertaining to patient age, length of stay, ICU admission, and trauma scores will be evaluated for possible trends/correlation between age and outcomes from trauma victims.

**Progress:** Preliminary data analysis has been performed. The study found a significant under-triage rate among elderly patients and significant differences among outcomes following trauma. An abstract has been submitted to the Army Surgical Symposium and the Washington State Chapter of the American College of Surgeons meeting. Investigators plan to continue further data analysis and preparation of a manuscript for publication in a peer reviewed journal.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206038	<b>Status:</b> Terminated
<b>Title:</b> Venous Distensibility Index as a Predictor of Radiocephalic Arteriovenous Fistula Maturation		
<b>Principal Investigator:</b> CPT Jason T. Perry, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD; LTC Benjamin W. Starnes, MC; COL Howard M. Cushner, MC; Leslie B. Schoneman, PA-C		
<b>Start - Completion:</b> 5 Jan 2006 - Jul 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 16 Jan 2007

**Study Objective:** Objective is to determine whether venous compliance, as measured by a venous distensibility index (VDI), is associated with an increased rate of arteriovenous fistula (AVF) maturation.

**Technical Approach:** 50 patients with end-stage renal disease referred to Vascular Surgery for consideration of permanent hemodialysis vascular access will be offered enrollment in this study. Venous distensibility index will be determined by modifying the preoperative ultrasound protocol already utilized in every dialysis candidate in whom an arteriovenous fistula is considered. In addition to collecting historic (e.g. duration and etiology of end-stage renal disease), physiologic (creatinine clearance, HbA1c), morphologic data (vein calibers, venous distensibility index), patients will be followed to determine the rate of maturation at six weeks and three and six months post-operatively. Maturation rate at three months will be considered the primary endpoint with maturation rates at six weeks and six months and fistula volume flow and arterial and venous wall thicknesses at one and six weeks and three and six months considered secondary endpoints. At this time, the data will be analyzed to determine whether a cutoff VDI can be established which segregates patients into mature versus failure to mature groups. Chi-square analysis or Fisher's exact test will be used to compare the groups.

**Progress:** This protocol was terminated during FY07. Three subjects enrolled and all had fistulas that failed to mature. Unfortunately, no meaningful data could be obtained from this small subset and the subject population was not great enough to warrant further research.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206061	<b>Status:</b> Ongoing
<b>Title:</b> Utilization of Genetic Testing and Counseling Among Patients with Hereditary Non-Polyposis Colorectal Cancer		
<b>Principal Investigator:</b> CPT Jason T. Perry, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 7 Feb 2006 - Jul 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 19 Jan 2007

**Study Objective:** To describe rates of utilization of genetic testing and counseling (GTC) among patients diagnosed with hereditary non-polyposis colorectal cancer (HNPCC) and further characterize use of recommended screening/surveillance studies after receiving GTC.

**Technical Approach:** Patients contained in the Madigan colorectal cancer database (from its inception in 1995 to present) and meeting the Amsterdam criteria II criteria will be extracted. The uptake of genetic testing and counseling will then be derived by reviewing patient medical records (including pathology results contained within the CHCS), and patient records from Medical Genetics. This study will further attempt to characterize patients' adherence to recommended screening guidelines and or surgical interventions follow testing and counseling in comparison to patients that did not accept testing or counseling.

**Progress:** This retrospective review of all patients treated at MAMC with a diagnosis of hereditary colon cancers remained ongoing during FY07 for continued data acquisition.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207074	<b>Status:</b> Ongoing
<b>Title:</b> Proteomic Analysis of Serum and Colonic Biopsy Specimens from Patients with Inflammatory Bowel Disease		
<b>Principal Investigator:</b> CPT Jason T. Perry, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Scott R. Steele, MC; CPT Vance Y. Sohn, MC; CPT Matthew J. Eckert, MC; Danielle L. Ippolito, PhD; CPT Lionel R. Brounts, MC		
<b>Start - Completion:</b> 12 Mar 2007 - Mar 2009	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to determine the protein expression (proteomic) profiles of patients with two forms of inflammatory bowel disease (IBD), ulcerative colitis (UC) and Crohn's disease (CD).

**Technical Approach:** By examining protein expression profiles of patients with inflammatory bowel disease (Crohn's disease or ulcerative colitis), this study will determine whether there is differential protein expression between the two diseases both to advance our understanding of the underlying pathogenesis and to more accurately diagnose patients with inflammatory bowel disease. Ten patients from each group (Crohn's disease and ulcerative colitis) will provide colonic biopsy and serum specimens which, in addition to routine clinical laboratory evaluation, will also undergo proteomic (surface-enhanced laser desorption/ionization time of flight mass spectrometry, SELDI-TOF MS) analysis to evaluate differential protein expression. Protein expression peaks constitute the outcome variables. Data will be analyzed by Student's t-test and area under the receiver operator characteristic curve.

**Progress:** This minimal risk protocol received initial approval by the Expedited Review Committee on 12 March 2007. An amendment was submitted and approved adding CPT Brounts as an associate investigator on 9 July 2007, and one subject enrolled during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204058	<b>Status:</b> Expired
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**Title:** Advanced/Combat Trauma Management Training Using Animal Models (Domestic Goat/Capra hircus, Pig/Sus scrofa)

**Principal Investigator:** LTC Robert M. Rush, MC

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** MAJ Alec C. Beekley, MC; LTC James A. Sebesta, MC; LTC Benjamin W. Starnes, MC; CPT Vance Y. Sohn, MC; LTC Matthew J. Martin, MC; CPT Jason T. Perry, MC; CPT Matthew J. Eckert, MC

**Start - Completion:**  
10 Mar 2004 - Mar 2007

**Funding:**  
Units via MOU

**Periodic Review:**  
8 Mar 2006

**Study Objective:** This protocol is intended to facilitate advanced and combat trauma management training of federally affiliated (e.g. DoD AC/RC, VA) physicians and ancillary medical personnel (e.g. nurse, physician's assistant, medic, medical/surgical technician, etc.).

**Technical Approach:** The protocol supports three levels of trauma management training, as follows: 1) Combat Relevant Trauma Management training for surgeons (CTM-S), focusing on preservation of life, limb, critical organ function, and casualty stabilization prior to medical evacuation for definitive care. 2) Combat-relevant Trauma Management training for physicians (CTM-P), focusing on preservation of life, limb, critical organ function, and casualty stabilization prior to medical evacuation for definitive care. 3) Combat-relevant Trauma Management training for ancillary medical personnel (CTM-NP), focusing on "hands-on" training of mission/duty-related trauma intervention procedures. Training associated with this protocol will utilize both inanimate (e.g. mannequin, cadaver, Simman, etc.) and live, anesthetized animal models. Whenever feasible, inanimate models will be used in place of live animals. Animal species used for this protocol will include goat and swine. The number of animals required is based on deployment of troops: Swine - Three to five personnel per animal, estimated that not more than 50 would be used per year. Goat - Three to five personnel per animal estimated that not more than 250 would be used per year.

**Progress:** Amendment #6 approved - Add procedure of teaching medics how to use the ez io device. Add management of open chest wound and Hemostasis of a groin arterial injury by proper application of Chitosan bandage and ChitoFlex. Change PI to Dr Robert Rush; Alec Beekley as AI. Add Dr Matthew Martin. Add Dr Sohn, Perry and Eckert as AIs. This protocol provided training for 340 medics, doctors and other medical support personnel in 18 training labs.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207075	<b>Status:</b> Ongoing
<b>Title:</b> Advanced/Combat Trauma Management Training Using Animal Models (Domestic Goat/Capra Hircus, Pig/Sus Scrofa)		
<b>Principal Investigator:</b> LTC Robert M. Rush, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Alec C. Beekley, MC; LTC Matthew J. Martin, MC; LTC James A. Sebesta, MC; CPT Vance Y. Sohn, MC; CPT Matthew J. Eckert, MC; CPT Jason T. Perry, MC; CPT Ryan K. Lehmann, MC		
<b>Start - Completion:</b> 12 Mar 2007 - Mar 2010	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to train federally affiliated (DoD/AC/RC/VA) Health Care Providers in advanced/combat trauma management skills essential to the maintenance of trauma/combat medical readiness. More specifically, this protocol encompasses duty/mission-specific combat-relevant trauma management training that is of limited availability to military HCPs in peacetime practice.

**Technical Approach:** This protocol is intended to facilitate advanced and combat trauma management training of federally affiliated physicians and ancillary medical personnel (nurse, physician's assistant, medic, medical/surgical technician). The protocol supports three levels of trauma management training, as follows: (1) Combat Relevant Trauma Management training for surgeons (CTM-S), focusing on preservation of life, limb, critical organ function, and casualty stabilization (damage control procedures) prior to medical evacuation for definitive care; (2) Combat-relevant Trauma Management training for physicians (CTM-P), focusing on preservation of life, limb, critical organ function, and casualty stabilization prior to medical evacuation for definitive care, and (3) Combat-relevant Trauma Management training for ancillary medical personnel (CTM-NP), focusing on "hands-on" training of mission/duty-related trauma intervention procedures. For the purpose of brevity, HCP (health care provider) will be used throughout this protocol to refer to physicians and ancillary medical personnel. Physician will refer to surgical and non-surgical medical doctors, unless specified otherwise. Training associated with this protocol requires completion of didactic training (based on HCP level of training) and inanimate model (e.g. mannequin, cadaver, SimMan, other simulation models, etc.) training prior to use of live, anesthetized animal models. Whenever feasible, inanimate models will be used in place of live animals. Animal species used for this protocol will include goat and pig.

**Progress:** This protocol received initial approval by the IACUC on 12 March 2007, and CIRO concurrence was received 22 June 2007. This protocol provided training for 340 medics, doctors and other medical support personnel in 18 training labs.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206101	<b>Status:</b> Ongoing
<b>Title:</b> ACOSOG Z6041: A Phase II Trial of Neoadjuvant Chemoradiation and Local Excision for uT2uN0 Rectal Cancer		
<b>Principal Investigator:</b> LTC James A. Sebesta, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC David E. McCune, MC; MAJ Jasmine T. Daniels, MC; MAJ Joseph P. Brooks, MC; MAJ Angela G. Mysliwiec, MC; LTC William B. Reece, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 10 Oct 2006 - Aug 2010	<b>Funding:</b> ACOSOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 12 Jun 2007

**Study Objective:** Objectives: To determine the rate of disease-free survival at 3 years in ultrasound-staged uT2uN0 rectal cancer patients treated with chemoradiation (CRT) followed by local excision (LE). To determine the rate of respectability with negative margins, procedure-specific morbidity and mortality, and quality of life in ultrasound-staged Ut2uN0 rectal cancer treated with neoadjuvant CRT followed by LE. To determine the feasibility of using molecular studies to assess surgical resection margins and tumor response to neoadjuvant CRT.

**Technical Approach:** This is a Phase II study of preoperative chemoradiation in patients with uT2uN0 rectal cancer. Patients will be identified and consented in the Surgical Oncology department. Prior to registration they will have a physical exam; lab work, scans and quality of life questionnaires (QOL). Eligible patients will be registered and begin treatment. Prior to chemoradiation patients will have biopsy samples collected and tumor tattooing to mark tumor measurement. Chemotherapy will be given as oral capecitabine on days 1-14 and 22-28, and IV oxaliplatin on days 1, 8, 22, and 29. Radiation therapy will be given concurrently according to standard therapy, five days a week, for weeks 1 through 5. During chemoradiation, patients will be followed with weekly exams, adverse advent assessment and lab tests. At week 12, patients will have local excision of remaining tumor, including collection of tissue specimens for correlative studies, and measurement of tattoo marks to mark response to treatment. Follow up will take place at Month 4 and every 4 months through Year 3. Patients will be followed every 6 months through Year 5. Follow-up procedures will include proctoscopy and CEA, endorectal ultrasound, and QOL.

**Progress:** Approved protocol documents were released to the study staff 10 October 2006, and a change in the role of PI from Dr. Sebesta to Dr. Brown was approved in March 2007. The study remains open to enrollment with no subjects identified as candidates for this trial thus far.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206114	<b>Status:</b> Completed
<b>Title:</b> Institutional Accuracy of 11- and 8- Gauge Vacuum-Assisted Core Biopsy of Mammographic Breast Lesions		
<b>Principal Investigator:</b> CPT Vance Y. Sohn, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 8 Aug 2006 - Dec 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine the accuracy of 11 and 8 gauge core needle sterotactic vacuum-assisted needle biopsy.

**Technical Approach:** A review of Breast pathway charts will be completed to identify patients with a diagnosis of atypical ductal hyperplasia on core biopsy who went on to open surgical biopsy. Of these, patients will be selected with a subsequent diagnosis of DCIS or invasive carcinoma and stratified according to the mammotome gauge. Correlation and analysis will be performed to see the accuracy of diagnosis of the 11 and 8 gauge mammotome between core needle biopsy and final excisional surgical biopsy. Results will be compared to published surgical literature.

**Progress:** This protocol was completed during FY07. Results: From June 1996 until July 2006, 4,579 CNBs were performed at our tertiary level medical facility. 78 of 88 (89%) of patients diagnosed with ADH on CNB with an 11-gauge vacuum-assisted needle underwent open surgical excision. Of these patients, 9 (11 %) were upgraded to ductal carcinoma in-situ (DCIS) while 5 (6%) had invasive cancer (I C) for a total underestimation rate of 17%. These results differ from our previously published series of 14-gauge CNB which revealed an underestimation rate of 36%. Mean number of passes obtained at time of biopsy, mean age of patients, and characteristic radiographic abnormality were similar for malignant and benign diagnoses. Conclusion: Eleven-gauge CNB technique reduces sampling error and improves accuracy, but does not eliminate the risk of missing an underlying malignancy. Surgical excision of ADH identified by CNB is required for definitive diagnosis.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206116	<b>Status:</b> Completed
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**Title:** Breast Papillomas in the Era of Stereotactic Core Biopsy

**Principal Investigator:** CPT Vance Y. Sohn, MC

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** CPT Joren B. Keylock, MC; LTC Tommy A. Brown, MC

**Start - Completion:**

15 Aug 2006 - Dec 2006

**Funding:**

DCI

**Periodic Review:**

N/A

**Study Objective:** To determine natural history of breast papillomas diagnosed during core needle biopsy.

**Technical Approach:** This will be a retrospective chart review of all patients with a diagnosis of papilloma on core needle biopsy. Data will be further analyzed with follow-up radiographic and other clinical notes. Those patients who underwent excisional biopsy will be compared to those who did not undergo immediate biopsy, but were rather follow-up serially with radiographs.

**Progress:** This protocol was completed during FY 2007. Results: From January 1994 until December 2005, 5,257 SCNBs were performed at our tertiary level medical center. 206 patients were diagnosed with 215 breast papillomas. 172 (80%) papillomas were benign, 25 (12%) were associated with atypia, and 15 (7%) were associated with malignancy. Three benign papillomas (1.7%) developed into cancer (1 infiltrating ductal carcinoma, 2 ductal carcinoma in-situ) over an average of 44 months. Average follow-up of those patients not undergoing excision for benign papilloma was 41 months although we had 92 patients with greater than 2 year follow-up and 57 patients with greater than 4 year follow-up. Of patients with atypia or malignancy associated with papilloma, there was a 26% and 87% associated rate of malignancy, respectively. Conclusions: Benign breast papillomas diagnosed by SCNB have an acceptably low risk of malignancy and do not need surgical excision. However, they should be considered high risk lesions which require serial radiographic monitoring (close follow-up). Papillomas associated with atypia or malignancy should continue to be excised.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207018	<b>Status:</b> Completed
<b>Title:</b> Surgical Treatment of Lobular Neoplasia		
<b>Principal Investigator:</b> CPT Vance Y. Sohn, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Garth S. Herbert, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 17 Nov 2006 - Dec 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to determine the need for further surgical intervention in patients diagnosed with lobular neoplasia during stereotactic core needle biopsy (CNB).

**Technical Approach:** Investigators will access the Madigan Breast Pathway, radiology, and pathology databases to identify all patients with a diagnosis of lobular neoplasia from core needle biopsy and compare those patients who underwent immediate surgical excision to those who did not. Of those patients who did not get immediate excision, we will obtain data from further radiographs or subsequent pathology specimens to see if these patients eventually developed malignancy in the breast of interest.

**Progress:** This retrospective review study has been completed and included 50 patient charts. As per protocol, no patient contact nor intervention was needed. This protocol and manuscript to be submitted for publication to the American Surgeon.

**Results:** From January 1994 to December 2005, 5,257 CNBs were performed at our tertiary level medical facility. Of patients with lobular neoplasia, 42 out of 50 (84%) patients had atypical lobular hyperplasia (ALH) while eight (16%) patients were diagnosed with lobular carcinoma in-situ (LCIS) on CNB specimen. There were no associated malignancies in 21 patients who underwent immediate surgical excision. Of those patients who were serially followed, four developed malignancies an average of 73 months after the sentinel diagnosis. Three out of the four (75%) malignancies occurred in the ipsilateral breast.

**Conclusion:** Patients with a diagnosis of lobular neoplasia by CNB should not routinely undergo an open surgical biopsy. Lobular neoplasia should only be considered a risk marker for future invasive breast cancer.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207035	<b>Status:</b> Completed
<b>Title:</b> Demographics, Treatment, and Early Outcomes in Penetrating Combat Vascular Trauma		
<b>Principal Investigator:</b> CPT Vance Y. Sohn, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 19 Dec 2006 - Dec 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To describe arterial and venous injuries, their management, and short term outcomes in a wartime hospital.

**Technical Approach:** This will be a retrospective analysis of a cohort of all trauma combat vascular injuries that were treated at the 31st CSH. Coalition patients with major vascular injuries will be identified in the Joint Theater Trauma Registry (JTTR). The 31st tourniquet database will be queried to determine whether limbs that were operated on are intact, or to count mortality as complication of procedure.

**Progress:** This retrospective analysis of a cohort of all trauma combat vascular injuries was reported completed in December 2007. Investigators found 153 patients with 218 vascular injuries, recorded from 1 January 2004 to 30 December 2004. Overall limb salvage rate was 80% while all cause mortality was 6%. Most vascular injuries were sustained by blast and fragmentation mechanisms. Not surprisingly, most vascular injuries were sustained in lower extremity vessels (57% arterial, 50% venous) with a high predominance of superficial femoral vessel injuries. Vascular injuries to the upper extremity were associated with a higher limb salvage rate (95%) compared to injuries to the lower extremities (71%). Variable follow-up data for 63 (41%) patients revealed 32 underwent further procedures outside the combat theatre, 12 of which were delayed amputations. Of all arterial injuries, 36% were primarily repaired, 34% were repaired with a vein interposition graft, 29% ligated, and 2% repaired with a prosthetic graft. Finally, a majority of venous injures (56%) were ligated.

## Detail Summary Sheet

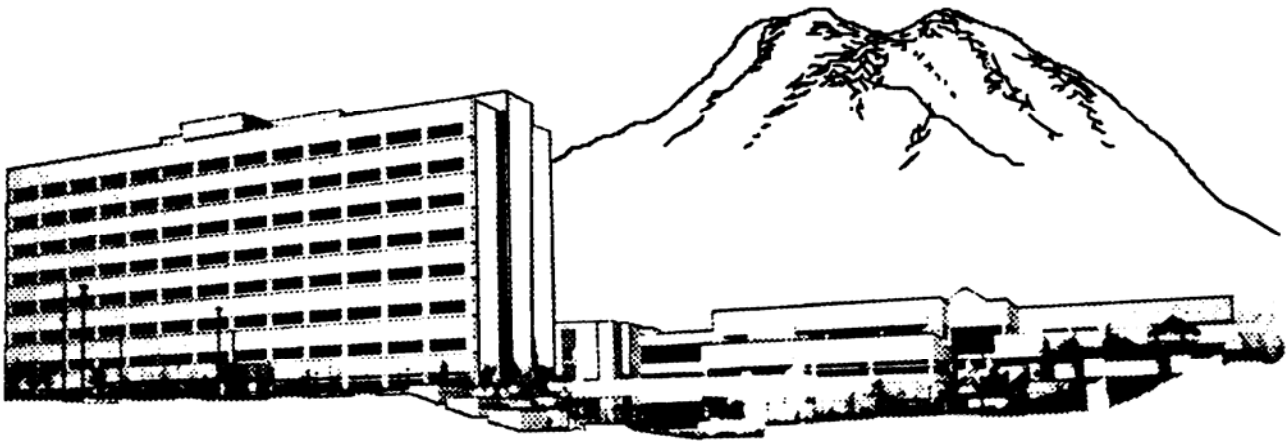
<b>Date:</b> 30 Sep 07	<b>Number:</b> 207038	<b>Status:</b> Completed
<b>Title:</b> Laparoscopic vs Open Colectomy for Colon Cancer: Results from a Large Nationwide Population-Based Analysis		
<b>Principal Investigator:</b> MAJ Scott R. Steele, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Matthew J. Martin, MC; LTC Tommy A. Brown, MC; LTC Robert M. Rush, MC		
<b>Start - Completion:</b> 9 Jan 2007 - Dec 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The purpose of this study is to analyze factors that affect the type of resection (laparoscopic versus open) performed for colon cancer and associated outcomes from a large nationwide database.

**Technical Approach:** This study is a retrospective registry review designed to analyze factors that affect the type of resection (laparoscopic versus open) performed for colon cancer and associated outcomes from a large nationwide database. We will retrospectively study all patients presenting to U.S. hospitals from January 1, 2003 to December 31, 2004 who underwent elective resection of colon cancer (not transverse colon or rectal cancer). Patients will be divided into groups based on method of operative resection (open versus laparoscopic) and these groups will be compared in terms of: demographics, length of hospital stay, discharge status, number and severity of pre-existing comorbidities, location and type of hospital in which repair was performed, hospital associated charges and in hospital mortality and identify any independent predictors of undergoing laparoscopic versus open resection.

**Progress:** This protocol was reported as completed in December 2007. Investigators identified 98,923 admissions (mean age 69.2 years). They were predominately Caucasian (81 %), had localized disease (63%), private insurance (56%), and had surgery performed in urban hospitals (87%). Laparoscopic resection was performed in 3,296 cases (3.3%) and was associated with a lower complication rate (18% vs. 22%), shorter length of stay (6 vs. 7.6 days), decreased need for skilled aftercare (5% vs. 11 %) and lower mortality (0.6% vs. 1.4%, all  $P < 0.01$ ). There was no significant difference in total hospital charges between the groups (\$34,685 vs. \$34,178,  $P = 0.19$ ). Independent predictors of undergoing laparoscopic resection were age  $< 70$  (odds ratio [OR] = 1.2,  $P < 0.01$ ), national region (Midwest OR = 1.9, West OR = 2.0,  $P < 0.01$ ) and lower disease stage (OR = 2.5,  $P < 0.01$ ). Ethnic category and insurance status showed no significant association with operative method ( $P > 0.05$ ).

**Conclusions:** Laparoscopy for colon cancer is associated with improved outcomes in unadjusted analysis and similar charges compared to open resection. We found no influence of race or payer status on the utilization of a laparoscopic approach.



## Detail Summary Sheets

Ophthalmology Service, Department of  
Surgery

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205090	<b>Status:</b> Ongoing
<b>Title:</b> Attitudes and Perceptions of Refractive Surgery Among ROTC Cadets Presenting for a Flight Physical and Self-Reported Barriers Towards Having Refractive Surgery to Correct Visual Acuity and Becoming Medically Qualified for Army Aviation		
<b>Principal Investigator:</b> CPT John H. Boden, MC		
<b>Department:</b> Surgery/Ophthalmology Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ John A. Edwards, MC; LTC Mark L. Nelson, MC		
<b>Start - Completion:</b> 2 Jun 2005 - Jun 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 16 May 2007

**Study Objective:** To identify attitudes and perceptions ROTC cadets applying for Army aviation have towards refractive surgery. This protocol will also attempt to identify any perceived barriers to receiving an exception to policy after having refractive surgery.

**Technical Approach:** This study will identify attitudes, and perceptions ROTC cadets have towards refractive surgery, in addition to identifying any perceived barriers cadets might have towards receiving an exception to policy after having refractive surgery. The study will include ROTC cadets who will undergo a flight physical medical examination in the year 2005. The sample population size will be approximately 600 ROTC cadets. Cadets will answer simple questions on a questionnaire given to them prior to having their flight physical. Analysis of answers provided on questionnaires will include correlation between subjects understanding of Army policy on refractive surgery, level of interest in becoming branch aviators, and understanding of the process entailed in receiving an exception to policy after having refractive surgery.

**Progress:** This protocol remains ongoing. A total of approximately 640 cadets applying for flight status during warrior forge 2005 completed the study questionnaire. Data from the questionnaires has been tabulated and data analysis is currently being worked on.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206124	<b>Status:</b> Completed
<b>Title:</b> The use of lidocaine gel prior to povidone - iodine antisepsis and its effect on microbial survivability		
<b>Principal Investigator:</b> CPT John H. Boden, MC		
<b>Department:</b> Surgery/Ophthalmology Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Mark F. Torres, MC; MAJ David M. Bushley, MC		
<b>Start - Completion:</b> 21 Sep 2006 - Oct 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to determine if the use of lidocaine gel prior to povidone-iodine antisepsis carries an increased risk of microbial survivability

**Technical Approach:** (1) A standard 0.5 McFarland suspension of *Staphylococcus epidermidis* will be diluted 1:10 with normal saline. A 0.001 ml loop will be used to inoculate each plate to give a standard  $1 \times 10^4$  to  $1 \times 10^5$  colony forming units on each blood agar plate. (2) A control group of 5 blood agar plates will be inoculated and labeled. (3) A group of 5 plates of inoculated blood agar will have lidocaine gel applied to the plate. The lidocaine gel will be allowed to drip across the agar plate as the plate is held vertically. After the lidocaine gel has covered the entire plate, the excess lidocaine gel will be wiped out using a sterile cotton tip applicator, and the plate will be stored upside down so that residual lidocaine gel can continue to drop off the agar plate. Each plate will be labeled. (4) A group of 5 inoculated blood agar plates will have lidocaine gel applied to the plate in the same manner as step 3. The plate will be placed upside down to allow excess gel to drip off the plate for 5 minutes. Dilute povidone-iodine 5% ophthalmic solution will be placed onto agar plate so that it covers the plate. The povidone-iodine solution will be left in place for 30 seconds and then the residual povidone-iodine solution will be dumped out of the agar plate. Each plate will be labeled. (5) A group of 5 plates of inoculated blood agar will have dilute povidone-iodine 5% ophthalmic solution placed onto agar plate and allowed to cover the plate for 30 seconds. After 30 seconds the povidone-iodine solution will be dumped out of the agar plate. Each plate will be labeled. (6) Steps 1 through 5 will be repeated 3 more times, but instead of using *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Haemophilus influenzae* will be used in each reiteration respectively. When *Haemophilus influenzae* is used standard chocolate agar will be used instead of blood agar. (7) The plates will be placed in a standard microbiology incubator used for aerobic culture, and microbial growth will be evaluated 24 hours later. If there is no growth after 24 hours, the plates will be reevaluated after another 24 hour time.

**Progress:** This laboratory protocol was completed during FY07 as planned. Results: In the *Staphylococcus epidermidis*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* groups, there was similarity in the amount of colony forming units in the lidocaine only, lidocaine and povidone-iodine, and control groups. In the *Haemophilus influenzae* series, the lidocaine with povidone-iodine group had fewer colony forming units than the control group. In all four groups, the povidone-iodine only group had the least amount of colony forming units, ranging from 0 to 3, and all were limited to the edges of the culture plate. A poster presentation was presented at the American College and Refractive Surgery conference in San Diego, California, April 2007. The PI is currently working on a paper to be submitted for publication.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206006	<b>Status:</b> Ongoing
<b>Title:</b> Virtual Ophthalmosurgical Simulator as a Valid Training Tool		
<b>Principal Investigator:</b> CPT Daniel J. Solverson, MC		
<b>Department:</b> Surgery/Ophthalmology Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Robert A. Mazzoli, MC; LTC William R. Raymond IV, MC; LTC Mark L. Nelson, MC; COL Kenneth S. Azarow, MC; COL Craig D. Hartranft, MC		
<b>Start - Completion:</b> 21 Oct 2005 - Feb 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 4 Oct 2007

**Study Objective:** To establish the validity of an ophthalmosurgical virtual reality simulator for intraocular surgery as an educational and assessment apparatus.

**Technical Approach:** All medical students, residents, ophthalmology staff physicians willing to participate will be recruited, have a visual acuity exam and be asked to complete a questionnaire to assess level of experience regarding microsurgery and handedness. All subjects will receive specific instructions on how to perform a navigation task on the EYESI virtual reality simulator by watching an instructional videotape. Each participant will complete several tasks including arranging small spheres near the retina and peeling a membrane off the retina. Main outcome measures in the arrangement task will be time to complete task as well as time to first error (such as a retinal hit) and participant microtremor throughout task. Each participant will also consecutively perform each task for a total of 15 times. Time intervals will be recorded between each consecutive task. Evaluations include: the relationship between the surgical experience and the task's completing time using ANOVA; the relationship between stereopsis and the task's completion time using Pearson correlation test; and the relationship between the surgical experience and the average tremor score using Pearson correlation test. To study the learning curve, the consecutive completion times for each subject and ANOVA will be evaluated to determine if there was a significant decrease in completion time throughout the 15 trials. For the membrane peeling task, the relationship between surgical experience and stereopsis with the number of retinal contacts, the task's completion time, and average tremor using ANOVA or Pearson correlation test will be evaluated, as appropriate.

**Progress:** Expert surgeons showed a greater facility with microsurgical tasks, but with repeated practice, novice surgeons showed significant improvement in all performance scores. The EYESI is able to distinguish between differing levels of ability, at least initially, and is a valid measure of basic skill.

Time performance is a simple, valid, and predictable measure of improvement, however should not be the sole measure of surgical skill. The skill of efficiency of movements, measured by the odometer score, demonstrates no learning curve for expert surgeons, however is rapidly acquired by novice surgeons. Further refinements of software modules may enhance the validity of this platform as both a part-task and ophthalmic procedure trainer. The EYESI could improve novice surgeon dexterity, with practice, to expert surgeon levels. Based on the study results, Madigan Army Medical Center constructed a formal resident training curriculum of surgical simulation in which novice performance is tied to gated benchmarks of expert performance. This protocol remains ongoing at MAMC.

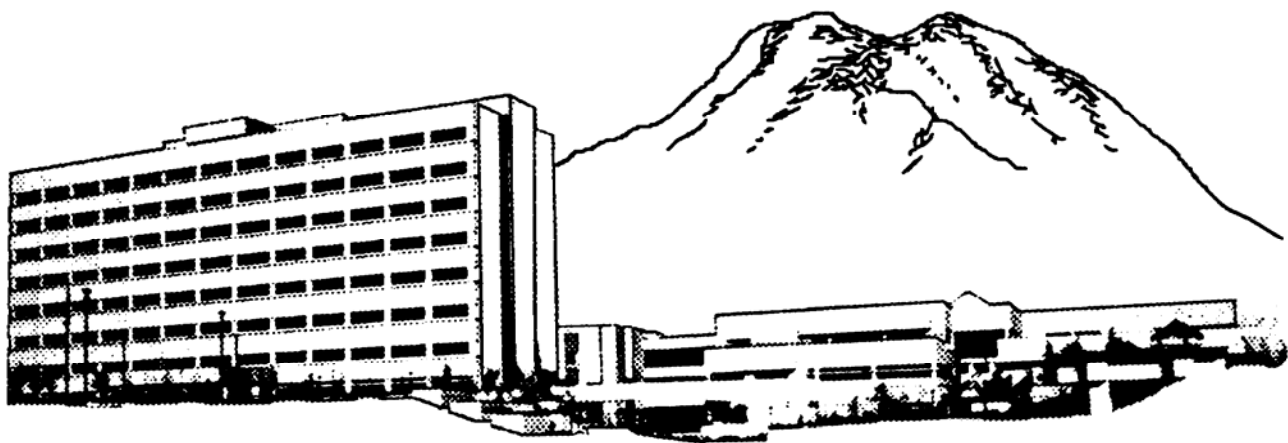
### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205083	<b>Status:</b> Terminated
<b>Title:</b> Ophthalmic Phentolamine Multiple Dose Clinical Trial		
<b>Principal Investigator:</b> LTC Mark F. Torres, MC		
<b>Department:</b> Surgery/Ophthalmology Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Aaron G. Amacher, MC		
<b>Start - Completion:</b> 17 Nov 2005 - Apr 2005	<b>Funding:</b> Ocularis Pharma via The Geneva Foundation	<b>Periodic Review:</b> 7 Jun 2006

**Study Objective:** Determine the effect on pupillary diameter of multiple doses of ophthalmic phentolamine (OP). Determine the effect on contrast sensitivity, glare sensitivity, and visual acuity of multiple doses of (OP). Determine the subjective benefits of multiple doses of OP. Determine the onset of action, the time of peak effect and the duration of the response of OP following multiple doses. Determine the safety and tolerability of OP following multiple doses.

**Technical Approach:** The Ophthalmic Phentolamine (OP) Multiple Dose Clinical Trial will study 12 otherwise healthy, 21-55 year old men and women who have had refractive surgery and have post surgical complaints of night vision problems. The study will be a randomized double-blinded placebo controlled crossover study with two periods. Each patient will receive two of three possible treatments: placebo, 0.2%, or 0.4% phentolamine. Pupil size, contrast sensitivity, glare sensitivity, accommodation, blood pressure and heart rate will be measured prior to application of OP. Following OP administration these variables will again be measured at intervals of one, four, and eight hours. Pre- and post-OP administered pupillary size, contrast sensitivity, visual acuity, glare sensitivity, subjective assessments, blood pressures and heart rates will be statistically compared in order to: (1) Determine the effect on pupillary diameter of multiple doses of ophthalmic phentolamine (OP). (2) Determine the effect on contrast sensitivity, glare sensitivity, and visual acuity of multiple doses of (OP). (3) Determine the subjective benefits of multiple doses of OP. (4) Determine the onset of action, the time of peak effect and the duration of the response of OP following multiple doses. (5) Determine the safety and tolerability of OP following multiple doses.

**Progress:** This protocol was terminated by the IRB Chair in September 2007, as the CRADA/SOW had expired in March 2007, and no glare patients had been identified since initial IRB approval was received in December 2005. Therefore, the IRB Chair determined that it was no longer feasible to conduct this research study as written.



## **Detail Summary Sheets**

Orthopedics Service, Department of Surgery

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206022	<b>Status:</b> Ongoing
<b>Title:</b> Accuracy of Reduction Utilizing Volar Fixation for Dorsally Displaced Fractures of the Distal Radius		
<b>Principal Investigator:</b> CPT Ivan J. Antosh, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC John G. DeVine, MC; COL Sean D. Ghidella, MC; CPT Llewellyn V. Lee, MC; CPT Joshua P. Herzog, MC		
<b>Start - Completion:</b> 8 Feb 2006 - Nov 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 25 Sep 2007

**Study Objective:** To determine the accuracy of a volar fixed angle plate in operatively treated distal radius fractures.

**Technical Approach:** This study will enroll the next 34 patients that present with a distal radius fracture who are selected by the treating physician to undergo surgical correction with a Hand Innovations DVR plate. All patients will undergo a preoperative and postoperative CT scan of their wrist. There will be no change in the operative approach, surgical technique or postoperative rehabilitation. Demographic and contact information will be gathered.

Radiographic measurements of the injury CT and post-op CT will be evaluated by three separate readers and the averages used for statistical calculations. The films will be evaluated for (1) radial height, (2) radial inclination (3) dorsal/volar angulation (4) articular step-off (5) articular gapping (6) degree of comminution using a visual analog scale, (7) presence or absence of distal radioulnar joint (DRUJ). The preoperative measurements will then be compared to the postoperative measurements utilizing the paired student T-test. The data from this study will be used to predict the accuracy of reduction with utilization of the Hand Innovations DVR plate.

**Progress:** This protocol remains open to enrollment with fifteen subjects enrolled since November 2006. One subject had bilateral distal radius fractures, which brought the number of data points to 16.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 200125	<b>Status:</b> Completed
<b>Title:</b> Subacromial Injection of Corticosteroids versus Ketoralac for Treatment of Shoulder Impingement Syndrome		
<b>Principal Investigator:</b> COL Edward D. Arrington, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Paul M. Ryan, MC; MAJ Bryant G. Marchant, MC; CPT Neil C. Vining, MC; COL (Ret) Patrick St Pierre, MD; MAJ Christopher J. Wilson, MC; CPT Brian K. Konowalchuk, MC		
<b>Start - Completion:</b> 5 Sep 2000 - Jun 2001	<b>Funding:</b> DCI	<b>Periodic Review:</b> 23 Aug 2005

**Study Objective:** To evaluate the difference in pain relief and functional outcome for subacromial impingement syndrome for patients who are treated with either a subacromial injection of corticosteroids or a subacromial injection of Ketoralac.

**Technical Approach:** This double-blind, randomized study will enroll approximately 40 patients with uncomplicated impingement syndrome for treatment with either subacromial corticosteroids or Ketoralac. Subjects with subacromial impingement will be given either 6cc 1% lidocaine with epinephrine and 40 mg Triamcinolone (Control) or 6cc 1% lidocaine with epinephrine and 60mg injectable Toradol (Test). Patient evaluation will be done at the time of injection and at 4 weeks post-injection.

**Progress:** This protocol was reported as completed in April 2007, with a total of 48 subjects enrolled in this study at MAMC. An abstract has not yet been submitted to DCI.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 201015	<b>Status:</b> Ongoing
<b>Title:</b> Biomechanics of Various Coracoclavicular Ligament Reconstruction Techniques		
<b>Principal Investigator:</b> COL Edward D. Arrington, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Kurtis L. Kowalski, MC; COL (Ret) Patrick St Pierre, MD; CPT Brendon R. Connolly, MC; MAJ Paul M. Ryan, MC; MAJ Creighton C. Tubb, MC; CPT Wendy J. Boucher, MC; CPT Joshua P. Herzog, MC		
<b>Start - Completion:</b> 15 Nov 2000 - Dec 2004	<b>Funding:</b> Mitek via The Geneva Foundation	<b>Periodic Review:</b> 4 Oct 2007

**Study Objective:** Test the strength and biomechanical characteristics of native and intact coracoclavicular ligament complexes as well as various reconstructive techniques for treating high-grade acromioclavicular joint separations.

**Technical Approach:** Thirty coracoclavicular bone-ligament-bone specimens will be harvested from fresh-frozen human cadavers. Unidirectional tensile loading will be performed with the Instron device. Tensile loading will be applied to the clavicle at a uniform rate until failure of the coracoclavicular ligament complex occurs. The coracoclavicular ligament will then be reconstructed using gracilis tendon, palmaris longus tendon, or SIS graft. The grafts will be looped multiple times under the coracoid process and over the top of the clavicle. It will be secured to itself with a #2 Ethibond suture. They will then be tested to failure as previously described.

Data will be obtained from the Instron device regarding tensile strength, load to failure, stiffness, and elongation to failure. Statistical analysis will be performed using a one-way ANOVA to determine differences between groups as well as Duncan's multiple range test to determine specific differences.

**Progress:** This bench research project remained ongoing during FY07. Since initiation of this protocol, numerous cadaver matched shoulders have been tested, both controls and experimentals. It appears the data is good and reproducible. The process of statistical analysis continues to determine the next step, including the testing of additional matched controls, and refinement of Instron techniques. Testing of additional experimental reconstructions has begun.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203036	<b>Status:</b> Completed
<b>Title:</b> Intramedullary Fixation of Displaced Acute Middle One-Third Clavicle Fractures		
<b>Principal Investigator:</b> COL Edward D. Arrington, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Karin A. Johnson, MC; CPT John J. McGuigan, MC; Steven D. Travers, MPT; LTC Craig R. Bottoni, MC; MAJ Eric L. Smith, MC		
<b>Start - Completion:</b> 18 Mar 2003 - Mar 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 27 Feb 2007

**Study Objective:** To determine the usefulness of intramedullary fixation of the treatment of 100% displaced middle one-third clavicle fractures. Compare the rates of union, nonunion, and malunion versus non-operative treatment.

**Technical Approach:** This study will randomize patients with acute displaced middle one-third clavicle fractures to either standard non-operative treatment or to open reduction and intramedullary pin fixation. The ultimate goal of this research is to obtain fracture healing with anatomic alignment, in order to promote an earlier return to full duty using a minimally invasive method of fracture stabilization. If successful, normal shoulder mobility and function will be restored faster and the patients can return to full activities sooner.

**Progress:** The parent TAMC protocol entitled "Acute Operative Stabilization Versus Nonoperative Management of Clavicle Fractures: A Prospective Randomized Study," was reported completed at TAMC in FY06. No work was conducted on this study at MAMC during FY07. Eighteen MAMC subjects participated; however, complete data sets could not be obtained on all subjects. No complications or adverse events occurred.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204051	<b>Status:</b> Ongoing
<b>Title:</b> Efficacy of Post-operative Hip Spica Wrap Dressing after Primary Hip Arthroplasty in Preventing Post-operative Wound Complications and Blood Transfusions		
<b>Principal Investigator:</b> COL Edward D. Arrington, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Aaron H. Hoblet, MC; MAJ James A. Hall, MC; CPT John J. McGuigan, MC; CPT Nathan T Boykin, MC		
<b>Start - Completion:</b> 8 Sep 2004 - July 2004	<b>Funding:</b> DCI	<b>Periodic Review:</b> 2 Mar 2007

**Study Objective:** To determine the efficacy of post-operative hip spica wrap dressing in primary hip arthroplasty in preventing wound complications and blood transfusions.

**Technical Approach:** Patients undergoing total hip arthroplasty or hemi-arthroplasty, electively or due to trauma, over the age of 18, male or female, are eligible to participate in this study. The next 20 patients who meet inclusion criteria will be randomly selected, after wound closure, to be placed in group A (standard wound closure with standard dressing and paper tape plus a hip spica wrap dressing) or Group B (the control group, standard wound closure with standard dressing of perforated cloth tape without the hip spica wound dressing). Data will be recorded pre-operatively to include medical comorbidities, height, weight, pre-albumin, albumin, hematocrit and post-operatively to include length of incision, amount of drainage per dressing, weight, the change in hematocrit, the need for a transfusion, length of hospital stay and any wound complications. Using the Student's T-test, this study will show a statistically significant decrease in wound drainage, decreased number of wound complications, decrease in length of hospital stay, smaller drop in the hematocrit and decrease need for transfusions.

**Progress:** No activity has occurred under this protocol, while searching for an orthopaedic research coordinator to facilitate data collection and a total joint surgeon to be in place prior to initiating enrollment of subjects.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206036	<b>Status:</b> Suspended
<b>Title:</b> Return to Full Duty after Anterior Cruciate Ligament Reconstruction in the Military Population		
<b>Principal Investigator:</b> COL Edward D. Arrington, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC John G. DeVine, MC; CPT Joshua P. Herzog, MC		
<b>Start - Completion:</b> 20 Dec 2005 - Jun 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8 Dec 2006

**Study Objective:** Objectives are to determine the rate of return to a soldier's pre-injury MOS after undergoing an anterior cruciate ligament (ACL) reconstruction and to identify risk factors to assist in predicting a decrease rate of return to full duty.

**Technical Approach:** A retrospective chart review of all 604 active duty patients who underwent an ACL reconstruction from 1994-2002 will be performed to identify potential predictors of poor outcomes, such as Age, Gender, MOS, time from injury to surgery, graft choice, intra-articular injuries (meniscal tear, meniscal treatment, chondral injuries, chondral treatment), duration of follow-up. Patients will be mailed questionnaires that will include four validated outcome instruments, a review of systems, questions regarding additional surgery, questions regarding any changes in social or demographic information. Patients will be asked what their pre-injury MOS was and if this was maintained post-rehabilitation (6 months); their current occupation; if they have ever undergone an MEB and the underlying condition that generated the MEB, and if they have a permanent profile for symptoms related to the operative knee. The primary outcome is the presence of an MEB, MOS change or Perm Profile as a result of symptoms related to the operative knee. This study will demonstrate the attrition rate in active duty soldiers after and ACL reconstruction and serve to identify predictors via a statistical model to predict who fails active duty ACL reconstructions.

**Progress:** This retrospective review of functional outcomes after ACL reconstruction has not yet been initiated, as a list of previous ACL reconstruction patients has not yet been obtained. The protocol remains ongoing to attempt to find a useable database with current contact information so that follow-up questionnaires can be mailed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206037	<b>Status:</b> Suspended
<b>Title:</b> A Retrospective Review of Injuries Sustained During Operation Iraqi Freedom and Operation Enduring Freedom Requiring Medical Evacuation to a Tertiary Medical Center		
<b>Principal Investigator:</b> COL Edward D. Arrington, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC John G. DeVine, MC; CPT John A. Guzzo, MC; CPT Joshua P. Herzog, MC		
<b>Start - Completion:</b> 21 Dec 2005 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8 Dec 2006

**Study Objective:** To provide an expanded casualty survey of evacuations to an Army Medical Center over the past 22 months via a retrospective chart review.

**Technical Approach:** Utilizing the daily OIF/OEF patient diagnosis report from Jan 2003-Nov 2005 approximately 1,085 soldier who were evacuated from OIF/OEF have been identified. A retrospective chart review using CIS, ICDB, ORMA and Dinpacs will be conducted. Demographic data to include age, sex, MOS and military rank will be collected. The patient diagnosis report and the detailed chart review will be used to document the type of injuries (Fracture, Neuro/vascular Damage, Amputation, Wound Care, Overuse Syndromes, Ligament Damage), Location of Injuries (Hand, Forearm, Arm, Shoulder, Foot, Leg/Ankle, Femur, Hip, Pelvis, Spine), Disease Non-Battle Injury vs. Combat Injury, Treatments, Number of days from injury, Pre-existing condition. Army Personnel Command will also be contacted to determine the normal demographical data for deploying soldiers out of the Pacific Northwest. This data will then be compared to the med-evac patient population to evaluate for a statistical difference. The data will be further evaluated by graphical means.

**Progress:** This is a retrospective review of patients with injuries sustained during Operation Iraq Freedom (OIF) and Operation Enduring Freedom (OEF) who required medical evacuation to Madigan Army Medical Center. Initial data collection was complete during FY06 and results presented in December 2007. The protocol remains ongoing to continue data collection and analysis.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206085	<b>Status:</b> Ongoing
<b>Title:</b> Pectoralis Major Repairs in Active Duty Soldiers		
<b>Principal Investigator:</b> COL Edward D. Arrington, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Jason A Grassbaugh, MC; CPT Ivan J. Antosh, MC; LTC John G. DeVine, MC		
<b>Start - Completion:</b> 8 May 2006 - Mar 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 17 Apr 2007

**Study Objective:** A retrospective review of all pectoralis major repairs performed at Madigan Army Medical Center from 2000 to 2006 with an objective to define expected results in terms of strength, functionality, pain, and ability to return to work among the active duty population.

**Technical Approach:** A list of all active duty soldiers who underwent operative repair of pectoralis major tendon tears from 2000-2006 will be gathered from operative records. Chart review will be performed in order to ascertain date of surgery, operative findings, repair methodology, rehabilitative plan and follow up visitations. After obtaining this data, patients will be contacted in writing in order to complete the DASH (Disability in arm, shoulder, and hand questionnaire). Results will be accumulated and analyzed.

**Progress:** This is a retrospective review of the functional outcome of pectoralis major rupture repairs in active duty Soldiers. Investigators attempted to contact sixteen Soldiers previously treated at MAMC over the past four years; 13 responses have been received. Investigators are in the process of analyzing this data, while attempting to contact the three remaining Soldiers.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207008	<b>Status:</b> Ongoing
<b>Title:</b> A Prospective, Randomized Study of Graft Selection in Anterior Cruciate Ligament Reconstruction		
<b>Principal Investigator:</b> COL Edward D. Arrington, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Sean D. Ghidella, MC; LTC John G. DeVine, MC; LTC Paul L. Benfanti, MC; LTC Lee A. McFadden, MC; Jill T. Eggers-Knight; CPT Nathan T Boykin, MC; CPT Christopher C. Hills; CPT Jason A Grassbaugh, MC; CPT Ivan J. Antosh, MC; CPT Aaron H. Hoblet, MC; CPT Josef K Eichinger		
<b>Start - Completion:</b> 14 Jun 2007 - Dec 2007	<b>Funding:</b> Regeneration Technologies, Inc. via The Geneva Foundation	<b>Periodic Review:</b> 23 Oct 2007

**Study Objective:** The objective of this study is to determine the optimal graft for patients undergoing an Anterior Cruciate Ligament reconstruction (ACL).

**Technical Approach:** This is a prospective, randomized study that will enroll the next 354 patients that present to the Orthopedic Clinic and require a primary ACL reconstruction. Patients will be randomized to one of six groups: (1) Autograft BTB, (2) Autograft hamstring, (3) Autograft Quadriceps Tendon, (4) Allograft Anterior Tibialis, (5) Allograft bone-patellar tendon-bone (BTB), and (6) Allograft adjustable length bone-tendon-bone. Prior to surgery subjects must complete a questionnaire that includes two validated outcome instruments, a review of systems, questions regarding additional surgery, questions regarding any changes in social or demographic information. The two validated outcome assessment tools include two sport-specific forms, the KOOS1 and IKDC2. A physical exam to evaluate their knee laxity, physical strength and motion will be conducted. The total follow up time will be 24 months with intervals appointments at 6 weeks, 3 months, 6 months, 12 months and 18 months. Pre-operative factors will be used to create a statistical model to predict which graft best serves possible ACL reconstruction candidates.

**Progress:** This greater than minimal risk protocol received initial IRB approval 24 October 2006, and following an administrative delay received final approval 14 June 2007. A total of 23 subjects enrolled in this study during FY07; twenty-two subjects have had treatment. One subject withdrew prior to treatment. Enrollment and follow-up will continue during FY08.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207080	<b>Status:</b> Ongoing
<b>Title:</b> A Comparison of ORTHOVISC® to Corticosteroid Injection in Shoulder Osteoarthritis		
<b>Principal Investigator:</b> COL Edward D. Arrington, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Sean D. Ghidella, MC; LTC John G. DeVine, MC; LTC Lee A. McFadden, MC; CPT Jon B. Christensen, MD, MC; CPT Ryan P Foley, MD, MC; Jill T. Eggers-Knight; MAJ David M Gloystein, MC; CPT Jason A Grassbaugh, MC; CPT Ivan J. Antosh, MC; CPT Nathan L Frost, MC; CPT Nathan T Boykin, MC; Steven D. Travers, MPT		
<b>Start - Completion:</b> 6 Jun 2007 - Feb 2009	<b>Funding:</b> ORTHOVISC via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The primary efficacy endpoints are (1) the change from baseline to six months in VAS pain score, and (2) responder analysis at six months where a responder is defined as a patient who achieves a 20 mm reduction in VAS pain. Secondary objectives are pain at the 12 week interval via VAS, responsiveness to change in OA of the GH joint at 12 weeks and 6 months via ASES scores, reduction in disability at 12 weeks and 6 months via SPADI, quality of live at 12 weeks and 6 months via SF-12 and, validation of the injection technique with guided imagery. Tertiary endpoints are rate of secondary treatments to index shoulder through 12 months, pain at 6 and 18 week intervals via VAS, responsiveness to change in OA of the GH joint at 6 and 18 weeks via ASES scores and, reduction in disability at 6 and 18 weeks via SPADI.

**Technical Approach:** This prospective, multicenter, double-blinded, randomized clinical study is designed to assess the safety and performance of ORTHOVISC injection for the treatment of pain due to osteoarthritis within the shoulder (glenohumeral) joint. Sponsors will use the data obtained in this trial to petition FDA for the indication of treatment of pain due to osteoarthritis and intended for use in the shoulder. Patients in this study will be randomized to receive either the ORTHOVISC injection (study treatment) or injection with corticosteroid/anesthetic alone (control treatment). Corticosteroid injections are the current standard of care for unrelieved pain caused by osteoarthritis in the shoulder joint. Additionally, this study is designed to help identify meaningful endpoints, validate the accuracy of the shoulder injection technique and to obtain patient health related information through appropriate questionnaires. All patients will be followed for a minimum of 6 months, with a phone call follow-up at the 12-month time point to collect any secondary procedures and event information. Both the patient and the principal investigator will be told at the 6 month visit which treatment the patient received. Up to 270 patients, both men and women will be enrolled at up to 8 research sites across the United States. Approximately 45 patients will be enrolled from Madigan Army Medical Center.

**Progress:** This greater than minimal risk protocol was initially approved by the IRB 27 March 2007, and received final approval 6 June 2007. Protocol documents were released to the study staff on 12 June 2007, and an amendment approved adding CPT Boykin as an associate investigator effective on 19 June 2007. This protocol was selected for inspection by the FDA during the week of 24-27 September. Thirteen subjects enrolled during FY07, and subject recruitment continues.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207095	<b>Status:</b> Terminated
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**Title:** Double-Blind, Multicenter Phase 3 Study Comparing the Efficacy and Safety of OMS103HP with Vehicle in Patients Undergoing Allograft ACL Reconstruction (Protocol #C03511)

**Principal Investigator:** COL Edward D. Arrington, MC

<b>Department:</b> Surgery/Orthopedic Surgery	<b>Facility:</b> MAMC
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**Associate Investigator(s):** COL Sean D. Ghidella, MC; LTC John G. DeVine, MC; LTC Lee A. McFadden, MC; MAJ Mark W. Manoso, MC; MAJ Cheryl L. Ledford, MC; MAJ David M Gloystein, MC; CPT Jason A Grassbaugh, MC; CPT Ivan J. Antosh, MC; CPT Nathan L Frost, MC; Steven D. Travers, MPT

<b>Start - Completion:</b> Terminated before final approval	<b>Funding:</b> Omeros Corporation via The Geneva Foundation	<b>Periodic Review:</b> N/A
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**Study Objective:** The primary efficacy objective is to assess whether patients randomized to the OMS103HP group have superior outcome as compared to patients randomized to the vehicle group in terms of the Knee Function Global endpoint. The secondary efficacy objectives are to assess whether patients randomized to the OMS103HP group have superior outcome as compared to patients randomized to the vehicle group in terms of the (1) Pain Management Composite, (2) Range of Motion Composite, (3) Knee Function Composite, and (4) Return to Work.

**Technical Approach:** This is a prospective, double-blind, randomized, vehicle-controlled, parallel-group study. A total of 280 patients (140 patients per group) are expected to be enrolled to allow for a roughly 10% dropout rate. Thus, approximately 250 evaluable patients (125 patients per group) undergoing primary unilateral allograft ACL reconstruction for a complete ACL tear occurring from two weeks to 18 months prior to the day of surgery are expected to complete this 90-day, multicenter study.

Patients will be randomized with equal probability to one of two groups, designated as the experimental group and the control group. The intended intervention in the experimental group is OMS103HP irrigation solution perfused through the knee joint during arthroscopic ACL reconstruction. The intended intervention in the control group is irrigation solution alone (vehicle irrigation solution) perfused through the knee joint during arthroscopic ACL reconstruction (standard care). Randomization is to be double-blinded relative to the clinical personnel, rehabilitation personnel, patients and the study sponsor, Omeros and its representatives.

The duration of the study for each patient is 3 to 3½ months, and includes a screening period of fourteen days (pre-operatively). Most postoperative clinic and rehabilitation evaluations will be performed over a 30 day period. A follow up clinic safety evaluation will be performed three months after the surgical procedure. Efficacy evaluations will be completed at the time of the Day 30 clinic visit and the twelfth rehabilitation visit. The Day 90 follow up clinic visit will evaluate safety only.

**Progress:** This greater than minimal risk protocol received initial IRB approval 22 May 2007, with a stipulation that the PI obtain study sponsor agreement with MAMC Physical Therapy plan to support the PT requirements in the protocol (per the impact statement filed with DCI), or find another pathway to comply with the PT requirements of the study. Final approval remained pending for several months to allow the PI time address this stipulation, however, the protocol approval process was administratively terminated, effective 6 November 2007, due to continued non-compliance with this IRB stipulation.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 207096		<b>Status:</b> Terminated	
<b>Title:</b> Double-Blind, Multicenter Phase 3 Study Comparing the Efficacy and Safety of OMS103HP with Vehicle in Patients Undergoing Autograft ACL Reconstruction (Protocol #C03512)					
<b>Principal Investigator:</b> COL Edward D. Arrington, MC					
<b>Department:</b> Surgery/Orthopedic Surgery				<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Sean D. Ghidella, MC; LTC John G. DeVine, MC; LTC Lee A. McFadden, MC; MAJ Mark W. Manoso, MC; MAJ Cheryl L. Ledford, MC; MAJ David M Gloystein, MC; CPT Jason A Grassbaugh, MC; CPT Ivan J. Antosh, MC; CPT Nathan L Frost, MC; Steven D. Travers, MPT;					
<b>Start - Completion:</b> Terminated before final approval		<b>Funding:</b> Omeros Corporation via The Geneva Foundation		<b>Periodic Review:</b> N/A	
<b>Study Objective:</b> The primary efficacy objective is to assess whether patients randomized to the OMS103HP group have superior outcome as compared to patients randomized to the vehicle group in terms of the Knee Function Global endpoint. The secondary efficacy objectives are to assess whether patients randomized to the OMS103HP group have superior outcome as compared to patients randomized to the vehicle group in terms of the (1) Pain Management Composite, (2) Range of Motion Composite, (3) Knee Function Composite, and (4) Return to Work.					
<b>Technical Approach:</b> This is a prospective, double-blind, randomized, vehicle-controlled, parallel-group study. A total of 280 patients (140 patients per group) are expected to be enrolled to allow for a roughly 10% dropout rate. Thus, approximately 250 evaluable patients (125 patients per group) undergoing primary unilateral autograft ACL reconstruction for a complete ACL tear occurring from two weeks to 18 months prior to the day of surgery are expected to complete this 90-day, multicenter study. Patients will be randomized with equal probability to one of two groups designated as the experimental group and the control group. The intended intervention in the experimental group is OMS103HP irrigation solution perfused through the knee joint during arthroscopic ACL reconstruction. The intended intervention in the control group is irrigation solution alone (vehicle irrigation solution) perfused through the knee joint during arthroscopic ACL reconstruction (standard care). The randomization is to be double-blinded relative to the clinical personnel, rehabilitation personnel, patients and the study sponsor, Omeros and its representatives. The duration of the study for each patient is 3 to 3½ months and includes a screening period of fourteen days (pre-operatively). Most postoperative clinic and all rehabilitation evaluations will be performed over a period of 30 days and a follow up clinic safety evaluation will be performed three months after the surgical procedure. Efficacy evaluations will be completed at the time of the Day 30 clinic visit and the twelfth rehabilitation visit. The Day 90 follow up clinic visit will evaluate safety only.					
<b>Progress:</b> This greater than minimal risk protocol received initial IRB approval 22 May 2007, with a stipulation that the PI obtain study sponsor agreement with MAMC Physical Therapy plan to support the PT requirements in the protocol (per the impact statement filed with DCI), or find another pathway to comply with the PT requirements of the study. Final approval remained pending for several months to allow the PI time address this stipulation, however, the protocol approval process was administratively terminated, effective 6 November 2007, due to continued non-compliance with this IRB stipulation.					

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205300	<b>Status:</b> Ongoing
<b>Title:</b> Stryker Biotech- OP-1 Bone Morphogenetic Protein, BMP-7 (HUD)		
<b>Principal Investigator:</b> LTC Paul L. Benfanti, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Edward D. Arrington, MC; LTC John G. DeVine, MC; COL Sean D. Ghidella, MC; MAJ James A. Hall, MC; CPT Glenn J. Kerr, MC		
<b>Start - Completion:</b> 8 Mar 2005 - Indef	<b>Funding:</b> Stryker via HDE	<b>Periodic Review:</b> 27 Feb 2007

**Study Objective:** Humanitarian Use Device

**Technical Approach:** OP-1 Bone Morphogenetic Protein will be used in patients that present with challenging and difficult to treat injuries that have a very poor success rate using normal methods and techniques. OP-1 represents the state of the art treatment of injuries that have challenged surgeons for decades, The success of this product lies in its use of a naturally occurring substance found in the human body to aid in the initiation of the natural cascade of events that promote bone healing. The incidence of adverse reactions associated with the implantation is less than 0.1%.

**Progress:** MAMC HUC approved continued use of this HUD, 27 February 2007, once a reporting mechanism was established. Physicians desiring to use OP-1 will first notify COL Arrington and the DCI Auditor about intended use, and provide two copies of the signed surgical procedure consent form indicating that the patient has been counseled about the potential use of OP-1, and two copies of the pre-op note. Four patients have been treated under this HUD during FY07.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205053	<b>Status:</b> Ongoing
<b>Title:</b> A Prospective, Randomized Clinical Investigation of the Cervitech, Inc. Porous Coated Motion Artificial Disc for Stabilization of the Cervical Spine at One Level between C3-C4 and C7-T1		
<b>Principal Investigator:</b> LTC John G. DeVine, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC John I. Iskandar, MC; COL Edward D. Arrington, MC; LTC Paul L. Benfanti, MC; MAJ Donny M. Melton, MC		
<b>Start - Completion:</b> 31 May 2005 - Feb 2012	<b>Funding:</b> Cervitech via Geneva	<b>Periodic Review:</b> 27 Feb 2007

**Study Objective:** The objective of this clinical study is to evaluate the safety and effectiveness of the PCM Porous Coated Motion Artificial Disc for treatment of degenerative disc disease compared to conventional ACDF in patients with DDD and neurological symptoms at one level between C3-C4 and C7-T1.

**Technical Approach:** This study plans to enroll 744 patients from areas across the US. Half of the patients will have surgery to remove the damaged disc and replace it with the study device (PCM). The other half of the patients will receive the current standard treatment; surgery to remove the damaged disc and then have the vertebrae fused together. This study will compare outcomes of disc surgery using the PCM Artificial Disc and the fusion surgery. Prior to surgery patients will have a physical exam, including x-rays, neurological testing, and either a MRI or CT scan (unless done in the past 12 months). A bone mineral density scan may be required to determine bone quality. The patient will also be asked to fill out surveys about neck symptoms, level of pain, and overall health. Patients will then be assigned to receive either the PCM or fusion procedure. The patients will not know which treatment they received until after surgery. Patients will be asked to return to the doctor's office for post-operative follow-up exams at 2-3 weeks, 6 weeks, 3 months, 6 months, 12 months, 24 months, and yearly thereafter until the study is completed, which may be 7 years after surgery. X-rays and patient surveys will be completed at these visits.

**Progress:** As of January 2007, 24 subjects have enrolled at this study at MAMC. One adverse event was reported due to an extra hospital day stay for post-operative nausea. The patient recovered and is continuing to be followed in the study. Screening and subject enrollment continues.

### Detail Summary Sheet

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<b>Date:</b> 30 Sep 07	<b>Number:</b> 206081	<b>Status:</b> Ongoing
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**Title:** Magnetic resonance imaging evaluation of adjacent segments after lumbar disc arthroplasty using the SB Charite implant

**Principal Investigator:** LTC John G. DeVine, MC

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<b>Department:</b> Surgery/Orthopedic Surgery	<b>Facility:</b> MAMC
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**Associate Investigator(s):** CPT Ivan J. Antosh, MC; CPT Brian J Woebkenberg, MC; COL Stephen M. Yoest, MC; CPT Gary V. Halversen, MC

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<b>Start - Completion:</b> 24 Apr 2006 - May 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 22 May 2007
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**Study Objective:** To determine whether or not magnetic resonance imaging is a viable imaging modality to evaluate adjacent segment after lumbar total disc replacement surgery using the SB Charite implant.

**Technical Approach:** Patients consented will have an MRI scan of their spine during a follow-up clinic visit, which will be evaluated by a radiologist as well as a member of the study staff. Meaningfulness of the scan will be determined by evaluating the ability to visualize the superior and inferior endplates as well as the disc space at both the superior and inferior adjacent levels.

**Progress:** This imaging study to look at the MRI findings at the treated and adjacent levels of the spine to determine the efficacy of the imaging modality and the affects the implant has on the quality of the imaging has enrolled 3 subjects. Subject accrual continues.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206082	<b>Status:</b> Ongoing
<b>Title:</b> Magnetic Resonance Imaging Evaluation of Adjacent Segments After Cervical Disc Arthroplasty Using the PCM Implant		
<b>Principal Investigator:</b> LTC John G. DeVine, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Ivan J. Antosh, MC; CPT Brian J Woebkenberg, MC; COL Stephen M. Yoest, MC; CPT Gary V. Halversen, MC		
<b>Start - Completion:</b> 24 Apr 2006 - May 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 22 May 2007

**Study Objective:** To determine whether or not magnetic resonance imaging is a viable imaging modality to evaluate adjacent segment after lumbar total disc replacement surgery using the SB Charite implant.

**Technical Approach:** Patients consented will have an MRI scan of their spine during a follow-up clinic visit, which will be evaluated by a radiologist as well as a member of the study staff. Meaningfulness of the scan will be determined by evaluating the ability to visualize the superior and inferior endplates as well as the disc space at both the superior and inferior adjacent levels.

**Progress:** This imaging study to look at the MRI findings after successful placement of an artificial cervical disc enrolled five subjects in FY07, and completed analysis of the findings. Subject accrual continues.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206120	<b>Status:</b> Ongoing
<b>Title:</b> A Single Blind, Multi-Center, Randomized, Prospective Clinical Study Comparing Optecure™ Autograft Extender to Autograft Only in Fusion of the Lumbar Spine		
<b>Principal Investigator:</b> LTC John G. DeVine, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Edward D. Arrington, MC; LTC Paul L. Benfanti, MC; MAJ Mark W. Manoso, MC; COL Sean D. Ghidella, MC; MAJ Eric M. Bluman, MC		
<b>Start - Completion:</b> 7 Dec 2006 - Feb 2009	<b>Funding:</b> Exactech, Inc. via The Geneva Foundation	<b>Periodic Review:</b> 25 Sep 2007

**Study Objective:** The primary objective of this study is to provide radiographic evidence that Optecure™ DBM, when used as an autograft extender, produces successful fusion in the lumbar spine. Secondary objectives include, but are not limited to, evaluating potential differences between the treatment groups in the occurrence of successful fusion, Oswestry Disability Index scores, SF-12 scores, and perceived pain as measured by Visual Analog Scales (VAS).

**Technical Approach:** Consecutive patients, at multiple centers, who are to be treated with lumbar fusion of 1 or 2 segments (i.e. 2 or 3 consecutive vertebrae) between L2 and S1, will be screened for participation in this clinical study. Following informed consent, approximately 150 subjects will be enrolled at multiple sites with 75 subjects expected to receive the treatment material (Optecure™ with autograft) and 75 the control material (autograft). Randomization will be accomplished at a 1:1 ratio (treatment vs. control). Investigators will remain blinded to the treatment type until decortication of the primary surgical site is complete. At that time the Randomization Envelope for the specific subject will be opened and will contain the Randomization Worksheet denoting the treatment to be used. The subjects will remain blinded to the type of treatment they receive until their participation in the study is complete (i.e., all follow-up visits are complete, subject is terminated from the study, or subject withdraws from the study). The vendor representative will bring the product to the OR for each case. Both the study material (Optecure) and the control material (autograft) are currently in use at Madigan Army Medical Center for spinal fusion. Follow-up will continue for 2 years following surgery. Radiographic, functional, patient health and pain data will be statistically compared between the two groups. A single, blinded radiologist will analyze fusion success at 6 months, 1 year, and 2 years postoperatively.

**Progress:** Approved protocol documents were released to the study staff 12 December 2006. Ten subjects enrolled during FY 2007; eight were randomized, had surgery and continue to be followed. Two subjects withdrew consent prior to randomization. No internal or external adverse events have been reported. Enrollment of new subjects continues.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207053	<b>Status:</b> Ongoing
<b>Title:</b> A Prospective, Multi-Center Clinical Study to Assess the Safety and Effectiveness of the Impliant TOPS™ System		
<b>Principal Investigator:</b> LTC John G. DeVine, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Edward D. Arrington, MC; CPT Ivan J. Antosh, MC; CPT Nathan L Frost, MC; MAJ Brett A. Schlifka, MC; MAJ Donny M. Melton, MC		
<b>Start - Completion:</b> 14 Mar 2007 - Jan 2012	<b>Funding:</b> Impliant, Ltd. via The Geneva Foundation	<b>Periodic Review:</b> 2 Jan 2008

**Study Objective:** The purpose of this multi-center, prospective, randomized, concurrently controlled clinical study (Pivotal) is to establish the safety and effectiveness of the TOPS™ System, used following decompression, in the treatment of lower back and leg pain with, or without spinal claudication, that results from moderate or severe lumbar spinal stenosis at one vertebral level between L3 and L5. Patients may also have, in addition to lumbar spinal stenosis, degenerative spondylolisthesis (Up to grade I) and/or facet arthrosis.

Primary safety and efficacy evaluation endpoints to determine individual patient success are (1) an improvement of at least 15 percent in the ODI at 24 months compared to baseline; (2) improvement of at least 20 mm in leg pain at 24 months compared to baseline using a VAS pain scale; (3) maintenance or improvement of neurological status; (4) no revisions, supplemental fixation, and removals; (5) absence of major device-related complications (device component degradation or breakage, device component separation or disassembly, device component loosening (including screw loosening)) requiring revisions, supplemental fixation, and removals; and (6) absence of spontaneous fusion in the investigational group and lack of fusion in the control.

Secondary outcome measurements that will be assessed include (1) Zurich Claudication Questionnaire scores, SF-36 scores, and VAS back pain score; (2) Adverse events; (3) time to recovery, work status, OR time, blood loss, and pharmaceutical use; (4) radiographic measurements (degree of stenosis, degree of spondylolisthesis, disc height, sagittal and coronal disc angle, coronal alignment, translational motions, Range of Motion (affected level and entire lumbar spine), disc health (affected and adjacent levels), fusion status, osteophyte formation, heterotopic ossification, disc darkening/signal intensity and device condition.

**Technical Approach:** A total of 350 - 450 patients will be enrolled then randomized in the study; 25 patients will be enrolled at MAMC. The first 40 randomized patients will be evaluated at the three month follow-up. Enrollment and site initiation will continue during the collection/evaluation and IDE supplement submission/review; however, patient surgery will not exceed 100 patients until FDA approval of this supplement is received. The DSMB will also perform a review of this interim safety analysis.

Patient demographic and medical information will be recorded. The patients will undergo a comprehensive clinical examination including neurological assessment, VAS (leg and back), Oswestry Questionnaire, ZCQ and SF-36, diagnostic studies, clinical scoring methods and radiographic assessment by plain and dynamic flexion/extension x-ray films, DEXA Scan, CT Scan and MRI. Patients recruited to the study will undergo implantation of the TOPS System or the control fusion procedure. The procedure involves the placement of four standard surface-blasted pedicle screws. A laminectomy and a medial facetectomy with adequate decompression of the neural elements necessary before the implant is connected to the pedicle screws. The operative procedure will be documented.

Patient follow-up will be evaluated immediately post-operatively and at discharge, 6 weeks, 3 months, 6 months, 12 months, and 24 months. Follow-up evaluation of the procedure will be based on the following clinical outcome parameters: Pain Relief will be evaluated using a VAS pain scale for evaluating leg and back pain; functional (disability/impairment) improvement of the patient will be evaluated using the Oswestry Questionnaire, Zurich Claudication Questionnaire (ZCQ, also referred to as the Swiss Spinal Stenosis Questionnaire) and SF-36; and Neurological Status (Reflex, Sensory, Muscle Strength, Straight Leg Raise and Femoral Stretch). Measurements will be taken on the radiographs at baseline and repeated at follow-up visits: Degree of Stenosis (baseline only); Sagittal and Coronal Disc Angle; Angular Range of Motion (flex/extend and lateral bending); Translational Motion; L1 - L5 Angle; Spondylolisthesis; Disc Height; Fusion Status; Osteophyte formation/heterotopic ossification; Disc degeneration/darkening; and Device Condition.

**Progress:** This greater than minimal risk protocol received initial approval by the IRB 23 January 2007, and final approval on 14 March 2007. No subjects have enrolled. Amendment #1 changes to the protocol lowering age group from 45 to 40, and request to add MAJ Melton as an associate investigator were submitted and approved during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205013	<b>Status:</b> Terminated
<b>Title:</b> A Double-blind, Randomized, Placebo-controlled Phase 2b Study to Establish the Effective Dose Range and to Evaluate the Safety of Chrysalin in Adult Subjects with a Fractured Distal Radius		
<b>Principal Investigator:</b> COL Sean D. Ghidella, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Christopher C. Hills; CPT Sarah D. Beshlian, MC		
<b>Start - Completion:</b> 3 Mar 2005 - Jan 2008	<b>Funding:</b> Orthologic via HM Jackson Foundation	<b>Periodic Review:</b> 24 Oct 2006

**Study Objective:** Primary Objective: To determine the time to removal of all rigid immobilization used to stabilize fracture after single injection of Chrysalin (1ug, 3ug, 10ug, 30ug) or placebo. Secondary Objective: To compare clinical assessment of bone healing, inflammation, edema, motion, and pain at fracture site, as well as to compare radiographic evaluation with global assessment of bone healing. Safety data will be collected on incidence and severity of emergent adverse events and laboratory assessments.

**Technical Approach:** This trial is a double-blind, randomized, placebo-controlled study to establish the effective dose range of a single percutaneous injection of Chrysalin (1ug, 3ug, 10ug or 30ug) in subjects being treated with surgical reduction of a distal radial fracture. At MAMC, the study will be conducted by the Orthopedic Service. 15-20 MAMC subjects may be enrolled for a total of 500 subjects to be enrolled in the study overall. Subjects will be consented and screened in the orthopedic service in collaboration with the research nurse. Subjects will then be scheduled for surgical reduction on a weekday, within a schedule that allows time for pre-study assessments to be done. Study assessments will include physical examination and history, baseline radiographs, pain questionnaire, CBC, serum chemistry, EKG, and serum HCG as appropriate, prior to study treatment. Chrysalin or placebo will be administered under fluoroscopic guidance in the OR as a single percutaneous injection, after surgical reduction of the fracture. Objective response to treatment will be measured with serial radiographs, grip strength and range of motion. Ongoing efficacy and safety evaluations will include, subject-rated pain scales and laboratory tests. Subjects will be followed by the Orthopedic Service for 52 weeks, including a referral to hand therapy for a minimum of 4 weekly sessions.

The primary analysis will be performed including all subjects who received their study injection and have had at least 8 weeks of follow-up. A secondary analysis will use a modified intent-to-treat sample including all subjects who have received study drug, regardless of follow-up. Safety analyses will include all enrolled subjects. Subjects who become pregnant will be followed to determine the outcome of the pregnancy.

**Progress:** This protocol was terminated in September 2007, with four subjects enrolled who completed study procedures. The study sponsor terminated the protocol when interim data analysis showed the study drug did not meet efficacy expectations compared to placebo. Three adverse events were reported during this study; one subject experienced two events (shortness of breath requiring hospitalization and hyperkalemia requiring hospitalization), and another subject was hospitalized to have a melanoma removed. Each event was assessed as unrelated to study participation, and possibly related to each subject's underlying disease.

### Detail Summary Sheet

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<b>Date:</b> 30 Sep 07	<b>Number:</b> 206009	<b>Status:</b> Ongoing
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**Title:** A Randomized Study of Volar Fixed-Angle Plate Fixation Versus Closed Management for Fractures of the Distal Radius

**Principal Investigator:** COL Sean D. Ghidella, MC

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<b>Department:</b> Surgery/Orthopedic Surgery	<b>Facility:</b> MAMC
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**Associate Investigator(s):** LTC John G. DeVine, MC; COL Edward D. Arrington, MC; LTC Paul L. Benfanti, MC; CPT Ivan J. Antosh, MC; MAJ Cheryl L. Ledford, MC; LTC Lee A. McFadden, MC; LTC Sandra Harrison-Weaver, SP; CPT Jorge E. Smith-Leon, SP; Elizabeth E. Miklos-Essenber; CPT Aaron H. Hoblet, MC; CPT Nathan L Frost, MC; CPT Aaron D. Dykstra, MC

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<b>Start - Completion:</b> 19 Apr 2006 - Apr 2007	<b>Funding:</b> Omeros Corporation via The Geneva Foundation	<b>Periodic Review:</b> 4 Oct 2007
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**Study Objective:** To determine the effectiveness of a volar fixed angle plate in distal radius fractures.

**Technical Approach:** The study will enroll 20 patients in each arm for a total of 40 patients. Subjects will have to meet the following inclusion criteria: 18-99 year old, Distal Radius Fracture, Active Lifestyle, Able to tolerate an operation., Articular Step-off <2mm, Articular Diastasis of <2mm, < 20 deg of dorsal angulation and dorsal comminution of >1/3 of the AP diameter of the radial shaft. Subjects will be excluded for volar oblique fracture (Volar Bartons), die punch fractures, associated DRUJ injury, and associated trauma (polytrauma). Subjects will be evaluated via the following outcomes: at time zero, 6 Weeks, 3 Months (M), 6 M, 12 M, 18 M and 24 M: Grip/Pinch strength, ROM, SF-36, Patient-rated wrist evaluation questionnaire (PRWE), DASH, Missed work days, Time (days) till Radiographic Union, and Complications.

**Progress:** This protocol has been open to enrollment since April 2006, with no subjects enrolled to date. Subject recruitment continues.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207052	<b>Status:</b> Completed
<b>Title:</b> A Randomized, Double-blind, Active-And Placebo-Controlled, Parallel Group, Multicenter Study To Evaluate The Efficacy And Safety of Multiple Doses of CG5503 Immediate-Release Formulation In Subjects Awaiting Primary Joint Replacement Surgery for End-Stage Joint Disease		
<b>Principal Investigator:</b> MAJ Mark W. Manoso, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Lee A. McFadden, MC; CPT Ivan J. Antosh, MC; CPT Nathan L Frost, MC; CPT Aaron H. Hoblet, MC; Jill T. Eggers-Knight		
<b>Start - Completion:</b> 15 Mar 2007 - Jul 2007	<b>Funding:</b> Johnson & Johnson via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective of this study is to determine the efficacy of CG5503 IR using the sum of pain intensity difference (SPID) over 5 days compared with placebo, and to assess the safety and tolerability of multiple doses of CG5503 IR over the double-blind treatment period in subjects who are eligible for elective primary total or partial joint replacement of the hip or knee due to chronic osteoarthritis.

The null hypothesis is that all CG5503 IR dosage efficacy results are equal to placebo based on 5-day SPID in the treatment of chronic pain from end-stage degenerative joint disease of the hip or knee. The alternative hypothesis is that at least one CG5503 IR dose effect will be different from placebo effect.

The secondary objectives are

- " Compare the effect of CG5503 IR with placebo in time to the first rescue pain medication during the double-blind treatment period
- " Evaluate the effect of CG5503 IR with the distribution of responder rates based on percent change from baseline in pain intensity (PI) for each of the time point (Day 2, 5, and 10)
- " Demonstrate the efficacy of CG5503 IR using total pain relief (TOTPAR) and sum of total pain relief and sum of pain intensity difference (SPRID) over 2, 5, and 10 days; and SPID over 2 and 10 days
- " Evaluate patient global impression of change (PGIC) of study treatment at the end of the double-blind treatment period
- " Evaluate the adverse event rates across treatment groups (especially nausea and vomiting)
- " Explore sleep quality and bowel movement using questionnaires
- " Explore the efficacy of oxycodone IR in comparison with CG5503 IR and placebo

**Technical Approach:** This is a randomized, double-blind, active- and placebo-controlled, parallel-group, multicenter, outpatient study to evaluate the efficacy and safety of multiple oral doses of CG5503 IR in treating chronic pain in subjects who are candidates for primary total or partial joint replacement surgery for end-stage degenerative joint disease of the hip or knee based on clinical and radiographic criteria defined by standard accepted guidelines appropriate in each country. A total of 624 subjects (156 per treatment group) will be randomly assigned to one of the following groups: (1) Placebo, (2) 50 mg CG5503 base IR, (3) 75 mg CG5503 base IR (includes a titration step of 50 mg for Day 1, and 75 mg for Days 2 to 10), or (4) 10 mg oxycodone IR.

Each subject will take the assigned treatment every 4 to 6 hours during waking hours throughout the double-blind outpatient treatment period. The study will be up to a maximum of 43 days in length. All opioid analgesics other than codeine, tramadol, or study drugs are prohibited within 28

days before screening and throughout the study. Codeine, tramadol, or combination products containing codeine or tramadol are allowed if taken intermittently up to 4 days each week for the previous 28 days before screening. The codeine or tramadol must be discontinued prior to the run-in period. Non-opioid analgesia will be allowed throughout the study if taken on a stable regimen for at least 28 days before screening. Subjects will be asked to stop any ancillary physiotherapy (e.g., hot/cold pack, magnets), massage therapy, physical therapy, or acupuncture at screening. The non-opioid component of combination products may be continued during the study.

All subjects will be asked to keep a diary. The diary will include a bowel movement questionnaire and a vomiting questionnaires, as well as entries for pain assessments. Efficacy, safety, pharmacogenomic (if consenting), and other evaluations will be performed at the times shown in the Time and Events Schedule.

**Progress:** This greater than minimal risk protocol received initial approval by the IRB 23 January 2007, and final approval on 15 March 2007. Multiple external adverse event reports were reviewed by the PI. A formal study sponsor close-out visit was conducted and the protocol reported completed 28 August 2007, with no subjects enrolled.

## Detail Summary Sheet

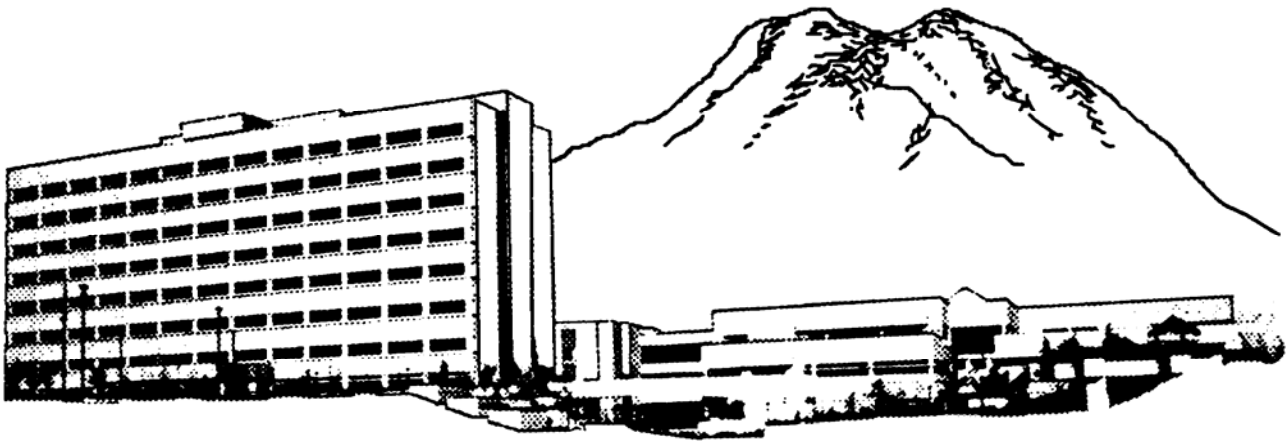
<b>Date:</b> 30 Sep 07	<b>Number:</b> 207002	<b>Status:</b> Completed
<b>Title:</b> Functional Outcome in Patients with Post-Operative Infections After Anterior Cruciate Ligament Reconstruction		
<b>Principal Investigator:</b> CPT Stephen A. Parada, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Edward D. Arrington, MC; LTC John G. DeVine, MC; CPT Jason A Grassbaugh, MC		
<b>Start - Completion:</b> 13 Oct 2006 - Oct 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objectives of this study are to (1) perform a retrospective chart review to gather data on the patients who experienced a post-operative infection after their anterior cruciate ligament reconstruction surgery at MAMC, and (2) obtain follow up from patients who had ACL infections after reconstructive anterior cruciate ligament surgery at MAMC over the past 6 years.

**Technical Approach:** In the first stage of this study, we will utilize inpatient charts to obtain data such as the time course of when patients experienced their post-operative infections and their clinical course that followed. We will obtain laboratory data by querying CHCS to trend WBC, ESR and CRP values. We will also obtain the dictated operative reports to assess how many repeat procedures were needed on these patients and to verify that no patients required a second reconstructive surgery due to the infection. Total number of ACL reconstruction is a number tallied annually by the orthopedic department in a manner which discloses no PHI and this will be reviewed to determine the total number of cases to provide a baseline gauge of the number of procedures that are done without any infectious complication.

In the second stage of the study, we will attempt to follow up with patients in a prospective manner. By using the last known contact information, we will try to reach the patients by phone in the manner that is represented on the phone survey. Patients that are contacted and agree to take part will be sent a survey in the mail to complete and return. Patients that live locally will be asked to come in for a brief knee examination that will include routine physical exam testing of the knee. This will consist of testing stability, strength and range of motion using described techniques that are all standard of care for a basic knee exam. Since all the patients in our study are active duty and prone to frequent relocations within the military, we are not expecting to be able to bring any of them in for the knee exam. For this reason, we are asking for a waiver of consent based on the impracticality of obtaining their consent in person if they are no longer in the area.

**Progress:** This protocol was completed during FY07. **Conclusions:** Orthopedics is a technology driven field with recent increase in the number of systems employed in routine orthopedic procedures and complexity of design. These systems may represent new challenges for standardized sterilization technique and may represent need for specialized material, equipment, and supply personnel to oversee cleaning and sterilization procedures. The bio-burden that had been introduced was discovered and corrected through the use of new wire brushes that were of smaller diameter. Once this issue had been identified and corrected, our institution had an immediate return of the pre-incident event rate of infection. Further, all these cases were managed with antibiotic therapy and serial irrigation and debridement procedures. In none of the six infections did a patient require a revision ACL reconstruction. The need to have ACL graft debridement has been reported in previous studies but was not required in our series of patients. Certainly similar outbreaks of this type warrant detailed evaluation of sterilization procedures.



## **Detail Summary Sheets**

Otolaryngology Service, Department of  
Surgery

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206030	<b>Status:</b> Ongoing
<b>Title:</b> Pediatric Bronchoesophagology Laboratory using Swine (Sus scrofa)		
<b>Principal Investigator:</b> LTC Mark E. Boseley, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Douglas M. Sorensen, MC		
<b>Start - Completion:</b> 8 Mar 2006 - Dec 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 10 Feb 2007

**Study Objective:** Skills used to remove foreign bodies in the airway or the esophagus are difficult to develop, taking years of training. To enhance and perfect these skills one must practice. This is best done in a laboratory setting with animal models. A laboratory allows the student to become familiar with the equipment used in pediatric endoscopy and reduplicates the real life setting closely. This ensures a level of technical proficiency that would enable the student to safely and successfully perform endoscopy and endoscopic procedures on children.

**Technical Approach:** Training Design: Animals, usually swine, are fully anesthetized by the certified veterinarian and his assistants. Under the supervision and instruction of board certified staff Otolaryngologists, bronchoesophagology procedures are performed on the animals by the residents. Procedures include direct laryngoscopy, rigid bronchoscopy, rigid esophagoscopy, and endoscopic removal of foreign bodies. The animals are sacrificed after all residents have completed training in the procedures.

**Anticipated Outcome:** Increased proficiency in broncho-esophagology procedures. The junior resident is better prepared to actually perform these procedures in pediatric patients. The more experienced residents are able to sharpen their proficiency on pediatric broncho-esophagology. **Clinical Application:** The more experienced residents are able to sharpen their proficiency in pediatric broncho-esophagology. The junior resident is better prepared to actually perform these procedures in pediatric patients.

**Progress:** This training protocol remains ongoing, with three training labs held during FY07, and 68 providers trained.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205050	<b>Status:</b> Ongoing
<b>Title:</b> Celecoxib Versus Oxycodone in Uvulopalatopharyngoplasty Surgery: A Comparison of Post-Operative Risks and Benefits		
<b>Principal Investigator:</b> CPT Joseph A. Chiara, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Douglas M. Sorensen, MC; CPT Matthew R. Grafenberg, MC; CPT Roy F. Thomas, MC		
<b>Start - Completion:</b> 28 Sep 2005 - Oct 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 23 Oct 2007

**Study Objective:** To determine if the drug valdecoxib (Bextra) is associated with less pain, nausea, bleeding and total cost as compared to oxycodone when used in the immediate pre- and post-operative period with uvulopalatopharyngoplasty (UPPP) surgery.

**Technical Approach:** All patients 18 years or older who are diagnosed as having heroic snoring or obstructive sleep apnea syndrome (OSAS) and deemed appropriate surgical candidates based on history and physical exam are eligible for inclusion in this study. There will be approximately 75 patients randomly assigned to three different study groups, (2 experimental and one control). These groups include (1) patients receiving a single pre-operative dose of Bextra and post-operative placebo, (2) patients receiving a pre-operative dose of placebo and post-operative Bextra (20 mg x 5d) and (3) patients receiving both pre-operative and post-operative placebo. Patients will be contacted 14 days after surgery with telephone calls to ensure completion of pain/nausea logs. A post-operative visit at 4 weeks will be scheduled.

The primary outcome variables will be duration/total amount of narcotic usage (oxycodone) and pain scores. Secondary outcome variables will include post-operative nausea and vomiting, bleeding and cost analysis. The number of days and total amount of narcotic usage will be calculated for each of the three study groups. Pain and nausea/vomiting will be measured by visual analog scales (VAS). Bleeding rates will be calculated based on those patients requiring intervention to stop bleeding either in the emergency room (ER) or the operating room (OR) by an ENT physician. Cost will be calculated based on price of medications used for each study group, additional unscheduled clinic visits and any ER/OR interventions performed.

**Progress:** This protocol remains ongoing at MAMC with no subjects enrolled thus far. Subject enrollment is expected to begin in FY08, with a new principal investigator.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205052	<b>Status:</b> Terminated
<b>Title:</b> MET™ Fully Implantable Ossicular Stimulator Clinical Trial Protocol		
<b>Principal Investigator:</b> MAJ James V. Crawford, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Carlos R. Esquivel, MC; LTC Dale A. Ostler, MS		
<b>Start - Completion:</b> 31 May 2005 - May 2008	<b>Funding:</b> DCI via Otologics, LLC	<b>Periodic Review:</b> 14 Aug 2006

**Study Objective:** To determine the safety and effectiveness of a Fully Implantable hearing device.

**Technical Approach:** The Fully-Implantable MET Ossicular Stimulator is an implanted prosthetic device, which bypasses the external auditory canal and mechanically stimulates the ossicles directly to take advantage of the patient's residual hearing. This system is intended to provide amplification with adequate gain, output and superior sound quality to that achieved with conventional, acoustic hearing aids. The target population includes patients who also want the convenience, and features of a fully implantable device which will provide them with amplification in situations where acoustic hearing aids were prohibited such as showering, swimming, sleeping, and various recreational activities.

A Phase I and II multi-site, clinical trial will be conducted with up to 90 patients at 15 investigational sites. The safety endpoints of air and bone conduction are assessed at 3, 6 and 12 month post implantation test intervals to demonstrate that residual hearing is not clinically, significantly affected by the implantation of the fully implantable device. The efficacy endpoints at each test interval are to demonstrate that the fully implantable hearing system is equal to or better than an appropriately fit air conduction hearing aid. The particular areas of comparison are for audibility of soft sounds, speech understanding in quiet and in noise, and perceived benefit by the patient as determined by a questionnaire. The approach to design and analysis has features of single-subject studies, reflecting repeated-measures, within-subjects design, wherein each subject acts as his/her own control.

**Progress:** This protocol was eventually terminated by the PI during FY07, no subject enrollment occurred.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205120	<b>Status:</b> Ongoing
<b>Title:</b> Complications and Audiologic/Tympanometric Findings in Children with Cleft Lip/Palate and Cleft Palate		
<b>Principal Investigator:</b> CPT Matthew R. Grafenberg, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Carlos R. Esquivel, MC		
<b>Start - Completion:</b> 18 Aug 2005 - Sep 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 10 Aug 2006

**Study Objective:** To determine if the surgical procedure of myringotomy with tympanostomy tube placement is associated with an increased risk of complications as compared with no surgical intervention in the cleft lip/palate and cleft palate population.

**Technical Approach:** This is a retrospective chart review of 88 patients, 18 years of age and younger, diagnosed with cleft lip/palate or cleft palate treated at MAMC over a 15-year period. Children with craniofacial anomalies without cleft/palate or cleft palate and those children with isolated cleft lip or cleft lip and alveolus will be excluded from the study. Patients will be divided into multiple groups based on type of cleft and whether surgical intervention with myringotomy and ventilation tube placement was performed. Comparisons will be made between groups with respect to complication types and rates, audiologic findings, tympanometric findings and functionality of tube as described above in the dependent variables section. The primary outcome variables will be complication rates, audiologic and tympanometric results. Other outcome variables will include the effect of cleft type on the need for at least one surgical procedure, effect of cleft type on the total number of surgical procedures, effect of cleft type on average age of 1st surgical procedure and average duration of functional tube based on both type of cleft and tube.

**Data Analysis:** Complication rates will be analyzed and compared on several different fronts. Patients will be divided into those that underwent surgical intervention and those that did not to determine if an association exists between surgical intervention and complication rate. In the group of patients where complications were noted to occur, the average number of ventilation tubes per patient will be calculated and compared to the group of patients that had ventilation tubes placed but no complications to determine if there is an association between increased number of procedures and complication rates. In addition, complication rates will be calculated for each type of tube and a comparison made between groups. Types of complications will also be calculated for each variety of tube and a comparison made between groups. Audiologic results will be reported as pure tone averages (PTA) as previously described. Overall PTA will be calculated for both patients undergoing surgical intervention and those that did not to determine if an association exists between hearing status and tube placement. In addition, both groups of patients will be further broken down according to cleft type to determine if this factor has any effect on hearing status. Those patients undergoing myringotomy with ventilation tube placement will be broken down into pre- and post-operative PTA values to determine if surgical intervention had an immediate short-term effect on hearing. In addition, long-term PTA at approximately 1 and 5 years after initial myringotomy with ventilation tube placement will be calculated for the surgical group (as previously described) and comparisons made to both the original pre-operative and non-surgical group PTA values to determine if surgical intervention has a long-term effect on hearing. Tympanometric results will be classified as normal or abnormal based on criteria previously described. Patients will once again be divided into two groups based whether they underwent surgical intervention. Comparisons between the two groups will be made to determine if an association exists between abnormal tympanograms and surgical intervention. In addition, each group will be further broken down by cleft type to determine if this variable had any effect on tympanogram results. Other outcome measures to be analyzed include the effect of cleft type on



the need for at least one surgical procedure, effect of cleft type on the total number of surgical procedures, effect of cleft type on average age of the 1st surgical procedure and the average duration of functional ventilation tube based both on type of cleft and tube.

**Progress:** This retrospective review protocol has completed data collection from 88 subject charts. Statistical analysis is being conducted. No further chart reviews will be required.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206020	<b>Status:</b> Completed
<b>Title:</b> Clinical Survey of Community Physicians: Post-Tympanostomy Tube Placement and Swimming Precautions/Treatment Otitis Media with Effusion		
<b>Principal Investigator:</b> CPT James M. Poss, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ James V. Crawford, MC		
<b>Start - Completion:</b> 30 Nov 2005 - Dec 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 2 Mar 2007

**Study Objective:** Objective: to determine the differences regarding Post-tympanostomy Swimming Precautions and treatment of Otitis Media with Effusion between Otolaryngologists, Pediatricians, and Family Practice physicians.

**Technical Approach:** Anonymous information will be placed into a database whereby simple statistical analyses can be performed (averages, means, Chi-squared) to look for statistical significance.

**Progress:** This protocol was reported as completed during FY07. Questionnaires were forwarded to 1,116 otolaryngologists, pediatricians and family practitioners in the Pacific Northwest. Over 200 practitioners responded to the questionnaires. The data was presented in poster format at AAO-HNS annual meeting in September 2006.

**Conclusions:** Recommendations for swimming precautions are not universal between the medical specialties that routinely see patients with tympanostomy tubes. Most primary care physicians and many otolaryngologists continue to prescribe water precautions to patients with tubes in place, despite published articles that have shown no reduction in the incidence of otorrhea from barrier devices or avoidance of swimming.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206125	<b>Status:</b> Ongoing
<b>Title:</b> Base of Tongue Reduction for Persistent Obstructive Sleep Apnea Using the Coblator II System: A Pilot Study		
<b>Principal Investigator:</b> CPT James M. Poss, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Samuel A. Spear, MC, USAF; MAJ Mark A. Criswell, MC		
<b>Start - Completion:</b> 17 Nov 2006 - Jun 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To evaluate the efficacy of coblator reduction of base of tongue in patients who have persistent obstructive sleep apnea (OSA) after prior palate surgery.

**Technical Approach:** Reduction of Base of Tongue with Coblator II plasma wand with integrated cable (8000 J delivered over 2 minutes). Three separate lesions will be made at each of three sites (midline and paramedian bilaterally). Three procedures will take place separated by a time period of at least 1 month.

**Progress:** Six patients have been enrolled and completed treatment. Data analysis is being conducted, as it became more difficult to enroll subjects, as most are receiving BOT treatment with palate surgery, which is part of the study's exclusion criteria. This protocol remains ongoing to complete data analysis.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204070	<b>Status:</b> Completed
<b>Title:</b> Perioperative Immunonutrition in Head and Neck Cancer		
<b>Principal Investigator:</b> LTC Douglas M. Sorensen, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Mary S. McCarthy, PhD; MAJ Brian J. Baumgartner, MC; LTC Susan G. Smith, AN; Katherine A. Simonson, RN; Vincent D. Eusterman, MD; CPT Sean M. Demars, MC; Evelyn B. Elshaw, RD, MS		
<b>Start - Completion:</b> 20 Jul 2004 - Oct 2005	<b>Funding:</b> Triservice Nursing Research Program via The Geneva Foundation	<b>Periodic Review:</b> 25 Apr 2006

**Study Objective:** (1) To determine the feasibility of providing perioperative nutritional support to a convenience sample of undernourished adults undergoing surgery for head and neck cancer. (2) To compare the difference in the nutritional parameters, albumin and prealbumin, between adult patients receiving IEN support or standard nutrition support administered before and after surgery for head and neck cancer. (3) To compare the difference in immune response measured by cutaneous delayed-type hypersensitivity testing, lymphocyte counts, and lymphocyte subset counts between adult patients randomized to receive either IEN support or standard nutrition support administered before and after surgery for head and neck cancer. (4) To compare the difference in surgical wound healing measured by visual inspection between adult patients randomized to receive either IEN support or standard nutrition support administered before and after surgery for head and neck cancer.

**Technical Approach:** On the day that consent is obtained demographic information will be recorded for age, gender, height, weight, diagnosis, risk factors, tumor category, and prior radiation therapy. Also, subjects will complete their section of the subjective global assessment (SGA) tool. Body fat analysis, indirect calorimetry (IC), and dietitian (RD) consultation will be performed. The speech language pathologist (SLP) will also examine the patient briefly to determine if any oral intake is safe. Subjects meeting criteria for inclusion into the study will be randomized to the experimental or control feeding group by the Research Associate.

Once the consent form is signed the surgery date will be noted and the first home visit will be set up with the patient for 8 days prior to surgery. Subjects will have baseline laboratory tests (albumin, prealbumin, T & B lymphocytes, and lymphocyte subsets) drawn on Day-8 or prior to initiating feedings (such as during the preoperative workup). A delayed cutaneous hypersensitivity test will also be placed by the immunization clinic prior to initiating the protocol. During the first home visit, any teaching given by the nursing staff regarding the feeding tube in the hospital will be reinforced and the RA will demonstrate proper use and care of the feeding device. The schedule for feedings (both oral and by feeding device) will also be reviewed with study groups. The RA will distribute the formula to all subjects when making the first home visit. Subjects will receive enough formula to administer >1 liter each day for 7 days. Containers will be labeled with the day and suggested time for infusion as well as numbered for accountability. The RA will also provide each subject with a diary. This diary will be used to record reasons for not following the feeding protocol, gastrointestinal symptoms, feelings/emotions, or questions to ask the investigators.

Each day for the next 6 days of preoperative feeding the RA will phone the subject and ask about adherence to the feeding protocol, difficulties with the feeding tube, or general concerns. Subjects will be reminded to save all formula containers and to bring them to the hospital the day of surgery. Postoperative follow-up visits occur with the ENT surgeon on a weekly basis. These visits will provide the perfect forum for the multidisciplinary research team to meet with the patient and assist with any care issues that have developed since discharge. On POD 15, 22, and 29, a wound

healing assessment will be performed by the physician and nurse jointly. On POD 29 the subject has completed the interventional study period and the PI/RA will record data regarding hospital outcomes, wound healing outcomes, and infectious complications.

**Progress:** This protocol was reported as completed in December 2006, and an abstract of findings submitted. Fifteen patients enrolled and completed the study. Perioperative nutrition support was found to be feasible and favorably accepted by patients and staff. Subjects did not vary in demographics at baseline. Preliminary analyses suggest a trend of less immune suppression (measured by CD4, CD8, and CD4:8 ratio) in the treatment group (TG) who received immune-modulating nutrition support for seven days pre- and post-operatively compared to the control group who received standard nutrition support. Patients were followed for three-weeks postoperatively to assess wound healing and infectious complications. No adverse events occurred during the study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206057	<b>Status:</b> Completed
<b>Title:</b> Review of Thyroid Cancer Treatment Outcomes at a Major Medical Center from 1996-2000		
<b>Principal Investigator:</b> CPT Samuel A. Spear, MC, USAF		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Douglas M. Sorensen, MC		
<b>Start - Completion:</b> 31 Jan 2006 - Jan 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** This will be a retrospective chart review of patients diagnosed with thyroid cancer at Madigan Army Medical Center from 1996 to 2000 to determine the effect of clinical and treatment factors on local tumor control, control of distant metastasis, recurrence, survival, and complications in all patients diagnosed and treated with differentiated thyroid carcinoma.

**Technical Approach:** All the records of patients diagnosed and treated for thyroid carcinoma at Madigan Army Medical Center from 1996-2000 will be identified through the MAMC pathology database, MAMC tumor-registry records and MAMC outpatient medical records and reviewed. Individual patient data will be collected with regards to age at diagnosis, gender, ethnicity, date of last known follow-up, initial FNA result, the presence of positive lymph nodes or metastases, the staging at diagnosis, the original tumor size, the histological type, the surgical treatment, any adjuvant therapy, any complications, recurrence date and location, treatment of the recurrence, mortality, cause of death, & disease free period. Data will be entered into an Excel spreadsheet for further evaluation and analysis.

**Progress:** This protocol was reported as completed in January 2007. Results: 82 patients were identified, 25 male and 57 female, with ages ranging from 17 to 77 years old and a mean follow-up of 5.1 years. 65 patients had papillary carcinoma, 15 patients had follicular carcinoma, one had medullary carcinoma and one had mucoepidermoid carcinoma of the thyroid. At diagnosis, 70 patients had disease confined to the thyroid, 12 had cervical lymph node metastases and two had distant metastases. Ten patients underwent thyroid lobectomy alone, nine had lobectomy followed by completion thyroidectomy, 46 had total thyroidectomy alone, and 16 had total thyroidectomy with neck dissections. One patient refused treatment. 45 patients received adjuvant 1131. Nine of the 82 patients had complications related to their treatment. Four of the nine were permanent. Four patients had local-regional recurrence and three patients had distant metastases. One patient died of their disease. Conclusions: Recurrent disease and distant metastases were associated with large tumor size, extra-capsular spread and positive cervical lymphadenopathy at time of diagnosis. Complication rates, recurrent disease rates and overall survival at this institution are comparable to national statistics and similar tertiary medical centers. Despite high survival rates, long term surveillance is warranted.

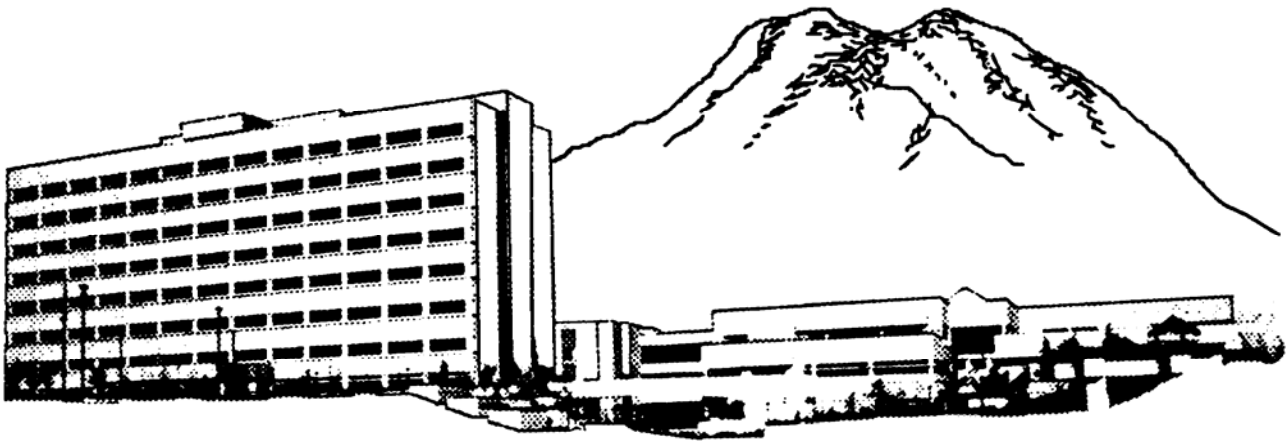
### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205009	<b>Status:</b> Ongoing
<b>Title:</b> Inferior Turbinate Reduction Comparing Turbinate Microdebrider, Coblation and Bipolar Cautery		
<b>Principal Investigator:</b> CPT Michael J. Wilhelm, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Roy F. Thomas, MC; CPT Jamie Hanson, MC; CPT Matthew R. Grafenberg, MC		
<b>Start - Completion:</b> 11 Mar 2005 - Apr 2006	<b>Funding:</b> Arthrocare via Geneva Foundation	<b>Periodic Review:</b> 23 Oct 2007

**Study Objective:** To determine the efficacy of inferior turbinoplasty using three accepted methods: turbinate microdebrider, coblation or submucous diathermy.

**Technical Approach:** This is a prospective, single blinded, randomized trial to compare use of a turbinate microdebrider, coblation and bipolar cautery device to determine if use of the microdebrider or coblator results in increased nasal volumes, decreased symptom scores and decreased nasal crusting when compared with turbinate bipolar. 90 patients, 30 per arm, will be recruited from patients referred to ENT with complaints of nasal obstruction. After informed consent is obtained, baseline evaluations will include history and physical exam, rhinoscopy, acoustic rhinometry and symptom scores. Patients will be randomized to receive turbinate reduction via turbinate microdebrider, coblator or bipolar. Follow up examinations will take place at 1 week, 2 weeks, 1 month and three months. Nasal crusting will be graded at 1 week, 2 weeks and 1 month. Symptom scores, rhinoscopy and acoustic rhinoscopy will be performed at 3 and 6 months. Comparisons will be made between baseline and postoperative data and between treatment groups. Results in change of volume from acoustic rhinometry will be evaluated with ANOVA to compare change in volume between the three arms of the study. Change in symptom scores between the three arms will be compared with the Kruskal Wallis test.

**Progress:** This protocol remains open to enrollment with eleven subjects enrolled during FY07. No adverse events have occurred.



## **Detail Summary Sheets**

Urology Service, Department of Surgery



## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 201107	<b>Status:</b> Completed
<b>Title:</b> A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of 10 mg Atrasentan in Men with Metastatic, Hormone-Refractory Prostate Cancer (M00-211)		
<b>Principal Investigator:</b> LTC Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Andrew C. Peterson, MC; CPT Jennifer M. Pugliese, MC; MAJ Keith J. O'Reilly, MC; MAJ Henry E. Ruiz, MC; CPT Jack R. Walter, MC; MAJ Leah P. McMann, MC; MAJ Sunil K. Ahuja, MC; MAJ Thomas L. Poulton, MC; COL Raymond A. Costabile, MC; MAJ Raymond S. Lance, MC; COL Robert C. Allen, MC		
<b>Start - Completion:</b> 4 Sep 2001 - Jul 2002	<b>Funding:</b> Abbott Labs via The Geneva Foundation	<b>Periodic Review:</b> 8 Jun 2006
<b>Study Objective:</b> 1) To evaluate the safety and efficacy as measured by time-to-disease progression. 2) To evaluate the effect of 10 mg Atrasentan on: PSA progression, Biochemical bone markers, Bone scan index, Survival and to evaluate the effect of the study drug on quality of life and performance status and to perform population pharmacokinetic analysis.		
<b>Technical Approach:</b> This is a phase III, multicenter, multinational trial evaluating the safety and efficacy of 10 mg Atrasentan in men with metastatic, hormone refractory prostate cancer. The men participating in this study have been diagnosed with hormone-refractory prostate cancer that has been treated with surgical and/or chemical castration but is now escaping androgen suppression as demonstrated by rising PSA. There must also be evidence of distant metastasis. The patient will then enter the screening phase, which will last 35 days and will include EKG, laboratory tests, medical history and physical examination. CT scan (or MRI) & bone scan will be performed. A copy of all scans will be sent to a Central Imaging Center within 2 weeks of collection. The patient will be randomized in a 1:1 ratio to receive either Atrasentan or a placebo (Day 1) via an Interactive Voice Response System (IVRS). Participants will be assigned a 4-digit study number and will be given study drug prior to leaving the clinic. Study medication will then be taken once a day at approximately the same time each day except for at Weeks 4 & 12 when a trough blood specimen will need to be drawn. At those two visits the patient will take the study medication after all laboratory specimens have been drawn. Participants will visit the clinic on Day 14, Weeks 4, 8, & 12, and every 6 weeks thereafter. At each visit the participants will be assessed for safety, clinical evidence of disease progression and will be dispensed study medication. They will be evaluated for disease progression by radiographic imaging every 12 weeks and as needed if participant experiences symptoms suspected to be related to disease progression. The subject will be considered to have completed the study if he has experienced an event of disease progression that has been confirmed by an independent reviewer, or is active in the trial when the double-blind treatment period ends (as defined by when 650 subjects have experienced confirmed events of disease progression). The subject will then be eligible to enter the open label extension study. If he declines to participate in the extension study, he will be asked to return for safety evaluation 30 days after their final visit. Subjects will be assessed for post-treatment survival at 3-month intervals after the last study visit. Someone who did not complete the study (premature withdrawal) will not be eligible to enter the extension study, but will be asked to continue coming in for visits as outlined above.		
<b>Progress:</b> This protocol was reported completed in May 2007. The study closed to enrollment in February 2003, with eight subjects consented, two screen failures, two withdrew consent, and four completed study treatment. No adverse events or changes to the protocol were submitted in FY07.		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 201113	<b>Status:</b> Terminated
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**Title:** A Phase III, Extension Study to Evaluate the Safety of 10 mg Atrasentan in Men with Hormone-Refractory Prostate Cancer (M00-258)

**Principal Investigator:** LTC Karen C. Baker, MC

<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC
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**Associate Investigator(s):** LTC Andrew C. Peterson, MC; CPT Jennifer M. Pugliese, MC; LTC Charles G. Henderson, MC; MAJ Michael J. Sebesta, MC; MAJ Keith J. O'Reilly, MC; COL Robert C. Allen, MC

<b>Start - Completion:</b> 4 Sep 2001 - Jul 2002	<b>Funding:</b> Abbott Labs via The Geneva Foundation	<b>Periodic Review:</b> 23 May 2006
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**Study Objective:** To evaluate the safety of 10 mg Atrasentan for the treatment of prostate cancer. In addition, the pharmacokinetic parameters of Atrasentan will be defined in a sub-population of subjects.

**Technical Approach:** This is a phase III, open label study evaluating the safety of 10 mg Atrasentan in men with hormone refractory prostate cancer. All men enrolled in this protocol must have successfully met all of the eligibility criteria for this trial and have completed one of the following Phase III trials:

M00-211: A Phase III, Randomized, Double-Blind, Placebo controlled Study Evaluating the Safety and Efficacy on 10 mg Atrasentan in Men with Metastatic, Hormone-Refractory Prostate Cancer

M00-244: A Phase III, Randomized, Double-Blind, Placebo Controlled Study Evaluating the Safety and Efficacy of 10 mg Atrasentan in Men with Non-Metastatic Hormone Refractory Prostate Cancer

Eligible men will receive a single, oral dose (soft gelatin capsule) of 10 mg Atrasentan before leaving the clinic (Day 1). They will then continue taking the same dose of study drug once a day at approximately the same time each day. The study participants will be asked to return to the clinic on study days 14, 28, at Week 12, and then every 12 weeks thereafter. Upon study completion subjects will be asked to come into the clinic for a final assessment, and will return again for a safety evaluation 30 days after the last dose of study drug. Blood will be drawn at every visit. Urine samples will be obtained at visit Day 1, Day 28, every 12 weeks and at final visit.

**Progress:** The Study Sponsor terminated this protocol in May 2007, after deciding not to pursue the use of Atrasentan monotherapy in prostate cancer. Six subjects enrolled, four completed the study, and the other two were discontinued. Two external adverse events were reported during FY07. No changes to the protocol were submitted.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 201121	<b>Status:</b> Completed
<b>Title:</b> A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of 10 mg Atrasentan in Men with Non-Metastatic, Hormone-Refractory Prostate Cancer (M00-244)		
<b>Principal Investigator:</b> LTC Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Andrew C. Peterson, MC; CPT Jennifer M. Pugliese, MC; MAJ Keith J. O'Reilly, MC; COL Robert C. Allen, MC		
<b>Start - Completion:</b> 11 Oct 2001 - Sep 2002	<b>Funding:</b> Abbott Labs via The Geneva Foundation	<b>Periodic Review:</b> 27 Jun 2006

**Study Objective:** Primary: To evaluate the safety and efficacy as measured by time-to-disease progression.

Secondary: (1) To evaluate the effect of 10 mg Atrasentan on: PSA progression, Biochemical bone markers, Bone scan index, (2) Survival, (3) To evaluate the effect of the study drug on quality of life and performance status and (4) To perform population pharmacokinetic analysis.

**Technical Approach:** This is a phase III, multicenter, multinational trial evaluating the safety and efficacy of 10 mg Atrasentan in men with metastatic, hormone refractory prostate cancer. The men participating in this study have been diagnosed with hormone-refractory prostate cancer that has been treated with surgical and/or chemical castration but is now escaping androgen suppression as demonstrated by rising PSA. There must also be evidence of distant metastasis. The patient will then enter the screening phase, which will last less than or equal to 35 days and will include EKG, laboratory tests, medical history and physical examination. CT scan (or MRI) & bone scan will be performed. A copy of all scans will be sent to a Central Imaging Center within 2 weeks of collection. After the patient has met eligibility criteria, the patient will be randomized in a 1:1 ratio to receive either Atrasentan or a placebo (Day 1) via an Interactive Voice Response System (IVRS). Study medication will then be taken once a day at approximately the same time each day except for at Weeks 4 & 12 when a trough blood specimen will need to be drawn. At those two visits the patient will take the study medication after all laboratory specimens have been drawn. The subject will be considered to have completed the study if he has experienced an event of disease progression that has been confirmed by an independent reviewer, or is active in the trial when the double-blind treatment period ends. The subject will then be eligible to enter the open label extension study. If he declines to participate in the extension study, he will be asked to return for safety evaluation 30 days after their final visit. Subjects will be assessed for post-treatment survival at 3-month intervals after the last study visit. Someone who did not complete the study (premature withdrawal) will not be eligible to enter the extension study, but will be asked to continue coming in for visits as outlined above.

**Progress:** This protocol was reported completed in May 2007. The study closed to enrollment in March 2003, with nine subjects consented, two screen failures, two withdrew consent, and five completed study treatment. Two external adverse events were reported during FY07. No changes to the protocol were submitted.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203035	<b>Status:</b> Ongoing
<b>Title:</b> A Multi-Institutional Pilot Study to Evaluate Molecular Markers in Urine and Serum in the Early Detection of Prostate Cancer		
<b>Principal Investigator:</b> LTC Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Keith J. O'Reilly, MC; MAJ Raymond S. Lance, MC; CPT Jack R. Walter, MC; CPT Dayne M. Nelson, MC		
<b>Start - Completion:</b> 28 Feb 2003 - Nov 2003	<b>Funding:</b> NCI	<b>Periodic Review:</b> 2 Jan 2008

**Study Objective:** The primary objective of this study is to examine whether the presence of tumor-specific gene promoter hypermethylation (e.g., GSTP1, Annexin II, CD44 and Caveolin 1) in serum and/or urine sediments can predict prostate cancer among patients referred to diagnostic biopsy. The secondary objective of this study is to explore whether the presence of tumor-specific gene methylation (e.g., GSTP1, Annexin II, CD44 and Caveolin 1) in core-needle biopsy specimens can predict subsequent disease status in patients who biopsy negative and develop cancer on subsequent biopsy within two years.

**Technical Approach:** 50 men who are between the ages of 40 and 75 years old and require prostate core needle biopsy will be enrolled in this pilot study here at MAMC. At the biopsy visit prior to the procedure the patient will be asked to provide a serum specimen. A 15-30 second prostate massage will be conducted and patients will be asked to provide a 30-50 ml urine specimen within 30 minutes of the massage. Each patient will undergo their scheduled core needle biopsy of the prostate. The number of biopsy cores taken will range from 8-12 which is Standard of Care at MAMC and will be left up to the discretion of the doctor performing the study. The concordance between gene methylation in the serum and urine, and diagnostic biopsy will be determined for all patients. Also methylation status of the tumor specimen will be determined for all cases who receive curative radical prostatectomy. Follow-up with patients will be determined by biopsy results. Length of study follow-up will be five years.

**Progress:** Although this protocol remains ongoing, there was no activity on the study during FY07. Enrollment closed in FY06 with 100 subjects enrolled. Follow up clinical data collection will be conducted for the next five years. Methylation assay of three genes in question has been completed on the biopsy cores of all 100 patients. The analysis of the urine samples is ongoing.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 204005	<b>Status:</b> Ongoing
<b>Title:</b> A Phase III, Randomized, Double-Blind, Placebo-Controlled Trial Evaluating the Ability of Risedronate to Prevent Skeletal Related Events in Patients with Metastatic Prostate Cancer Commencing Hormonal Therapy, Protocol #GU02-41			
<b>Principal Investigator:</b> LTC Karen C. Baker, MC			
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Andrew C. Peterson, MC; LTC Charles G. Henderson, MC; MAJ Michael J. Sebesta, MC; MAJ Jasmine T. Daniels, MC; LTC David E. McCune, MC; MAJ Angela G. Mysliwiec, MC; CPT Jennifer M. Pugliese, MC; CPT Dayne M. Nelson, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC			
<b>Start - Completion:</b> 29 Jan 2004 - Oct 2004	<b>Funding:</b> Hoosier Oncology Group via The Geneva Foundation	<b>Periodic Review:</b> 25 Sep 2007	
<b>Study Objective:</b> (1) To evaluate the ability of a daily oral dose of 30 mg risedronate as compared with placebo to prevent skeletal complications in patients undergoing androgen deprivation for metastatic prostate cancer by measuring the time to a skeletal-related event (SRE). (2) T evaluate a daily oral dose of 30 mg risedronate compared to placebo in patients undergoing androgen deprivation for metastatic prostate cancer with respect to the following: (a) The rate and the duration of the serological response by measuring the changes in prostate-specific antigen (PSA) levels, (b) The effect on tumor response by measuring the response rate after 6 months of therapy by radiographic means. (c) Time to development of hormone refractory disease. (d) The changes in biochemical markers of bone turnover. (e) Overall survival. (f) The safety and the tolerability as determined by frequency and severity of treatment-emergent adverse events.			
<b>Technical Approach:</b> This is a randomized, placebo-controlled, double-blind, multicenter, stratified, 2-arm study. Up to 360 evaluable subjects will be enrolled at approximately 50 study sites. After stratification based on age, performance status, and severity of metastatic disease, subjects will be randomized at a 1:1 ratio to the following treatment arms: (a) Daily risedronate combined with androgen deprivation, and (b) Daily oral placebo combined with androgen deprivation The study population will consist of prostate cancer subjects with metastatic bone disease for whom androgen-deprivation therapy is planned. Subjects will be registered to the study within 3 days before beginning risedronate or placebo and may begin androgen-deprivation therapy 7 days before beginning risedronate or placebo. The subject will receive treatment of one 30-mg tablet/placebo oral per day every morning. Subject is to take risedronate/placebo with 6-8 oz of water 30 minutes before the first food or drink of the day and should not lie down for 30 minutes after taking. Subjects will receive concomitant treatment with calcium carbonate at a dose of at least 500 mg orally per day every evening. Subjects will receive concomitant treatment with vitamin D at a dose of at least 400 IU. Subjects will remain in the study for at least 12 weeks, but may continue for 2 years or longer depending on progression of disease. They will be seen in the clinic every 4 weeks for the first 12 weeks and every 12 weeks thereafter.			
<b>Progress:</b> This protocol closed enrollment in August 2005, with four subjects enrolled. One subject was reported as lost to follow-up, and one subject remains active on study treatment. Study Sponsor looks to close this protocol by end of 2007. One external and one internal adverse event (carbuncle) were reported during FY07. Requests to add four new associate investigators were also submitted and approved.			

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204091	<b>Status:</b> Ongoing
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**Title:** A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate AMG 162 in the Treatment of Bone Loss in Subjects Undergoing Androgen-Deprivation Therapy for Non-Metastatic Prostate Cancer

**Principal Investigator:** LTC Karen C. Baker, MC

<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC
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**Associate Investigator(s):** LTC Andrew C. Peterson, MC; CPT Dayne M. Nelson, MC; CPT Jennifer M. Pugliese, MC; MAJ Michael J. Sebesta, MC; LTC Charles G. Henderson, MC; CPT Jack R. Walter, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC; CPT Brian J. DeCastro, MC; Dieter Kirchheim, MD

<b>Start - Completion:</b> 5 Oct 2004 - Aug 2006	<b>Funding:</b> Amgen, Inc. via The Geneva Foundation	<b>Periodic Review:</b> 22 May 2007
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**Study Objective:** Primary objective is to determine the treatment effect of AMG 162 compared with placebo on lumbar spine bone mineral density (BMD) in men with non-metastatic prostate cancer undergoing Androgen Deprivation Therapy. Secondary objectives are to assess the effect of AMG 162 compared with placebo on the vertebral and non-vertebral fracture incidence, BMD in total hip and femoral neck and to assess the safety and pharmacokinetics of AMG 162 in this population.

**Technical Approach:** This is an international, multi-center, randomized, double-blind, placebo-controlled study in subjects with non-metastatic prostate cancer undergoing androgen deprivation therapy (ADT). Approximately 968 subjects at approximately 150 sites in North America and Europe will be randomly assigned to receive placebo or AMG 162 in a 1:1 allocation ratio. The randomization schedule will be stratified based on age group ( $\leq 70$ ,  $> 70$  years of age), and duration of ADT with GnRH agonist, or orchiectomy at the time of study entry (0-6 months vs.  $> 6$  months). Subjects will participate in the study for 24 months. There is a planned interim analysis after subjects complete their one-year (12 month) study evaluation period. Once a subject has been determined eligible to participate in the study written consent must be obtained prior to screening for eligibility. Screening assessments include obtaining a medical history, physical examination, bone scan, radiographs, bone densitometry, and collection of blood for hematology and chemistry. Eligible subjects will return to the site within 28 days of screening for the baseline (day 1) visit, during which baseline-related assessments will be done and subjects randomized. Subjects will return at months 1, 3, 6, 12, 15, 18 and 24 for study related procedures and evaluations. All subjects will take daily calcium (1 gram) and vitamin D (at least 400 IU). All subjects will receive the same volume of study medication (AMG 162 vs. placebo) subcutaneously every 6 months. This study will also explore the effect of AMG 162 on PSA, overall survival, and subject reported outcomes (subject questionnaires).

**Progress:** This protocol closed to enrollment in April 2005, with thirteen subjects consented. Three subjects failed screening, and one withdrew consent. The protocol was extended to 36 months; of the remaining nine subjects, five decided to withdraw consent to continue treatment for 36 months. The protocol remains ongoing to continue study treatment for four subjects.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204120	<b>Status:</b> Ongoing
<b>Title:</b> The Effect of Flexible Cystoscopy on the Serum PSA Values		
<b>Principal Investigator:</b> LTC Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Brian J. DeCastro, MC; MAJ Mark I. Anderson, MC; LTC Andrew C. Peterson, MC; CPT Jennifer M. Pugliese, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC		
<b>Start - Completion:</b> 2 Feb 2005 - Nov 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 4 Oct 2007

**Study Objective:** To determine the affect of flexible cystoscopy on serum PSA values in male patients with prostates.

**Technical Approach:** Free and total PSA values will be obtained in 100 males ages 20 to 79 undergoing flexible cystoscopy to evaluate the effect of flexible cystoscopy on serum PSA values. Because PSA is an important screening test for prostate cancer in men aged 40 through 79, the number of study participants age less than 40 will be limited to 10 participants each for the age groups 20 to 29 and 30 to 39. All men will be volunteers who are already scheduled to undergo flexible cystoscopy. A serum sample for free and total PSA will be drawn up to 1 hour before flexible cystoscopy and will be the baseline value. Serum samples will be drawn again at 1 hour after cystoscopy and the day following cystoscopy. If interval analysis after 30 patients shows no clinically significant difference between the second and third serum samples, the third sample will be eliminated. The PSA values before and after cystoscopy will be compared with a paired t-test or the Wilcoxon signed-rank test. Additional variables that could influence the change in PSA values to include, but not limited to, age, race/ethnicity, prostate size, and reason for cystoscopy will be recorded and analyzed. Multivariate analysis will be applied once univariate analyses are completed.

**Progress:** This protocol closed enrollment during FY07, with 40 subjects enrolled. The study remains ongoing to complete and submit a final manuscript.

### Detail Summary Sheet

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<b>Date:</b> 30 Sep 07	<b>Number:</b> 205006	<b>Status:</b> Ongoing
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**Title:** A Randomized, Double-Blind, Placebo-Controlled, Multicenter Efficacy and Safety Study of Toremifene Citrate for the Prevention of Bone Fractures in Men with Prostate Cancer on Androgen Deprivation Therapy (Protocol #G300203)

**Principal Investigator:** LTC Karen C. Baker, MC

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<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC
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**Associate Investigator(s):** LTC Andrew C. Peterson, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC

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<b>Start - Completion:</b> 20 Jan 2005 - Jan 2007	<b>Funding:</b> GTx, Inc. via The Geneva Foundation	<b>Periodic Review:</b> 25 Sep 2007
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**Study Objective:** Primary Objective: To assess the efficacy of toremifene in the prevention of bone fractures in men with prostate cancer on androgen deprivation therapy as measured by semi quantitative assessment of vertebral fractures. Secondary Objectives: (1) To assess the safety profile of toremifene in subjects on androgen deprivation therapy (ADT) for the treatment of prostate cancer. (2) To assess the effect of toremifene on the incidence of clinical fragility fractures. (3) To assess the effect of toremifene on bone mineral density (BMD) of the lumbar spine as assessed by DEXA scan. (4) To assess the effect of toremifene on BMD of the femur as assessed by DEXA scan. (5) To assess the effect of toremifene on the incidence, frequency and severity of hot flashes. (6) To assess the effect of toremifene on the incidence and severity of gynecomastia. (7) To assess the effect of toremifene on quality of life.

**Technical Approach:** In a double-blind fashion, qualifying subjects will be equally randomized into one of two treatment groups. Up to 600 subjects will be randomly assigned to receive 60 mg toremifene citrate as two 40 mg tablets and up to 600 subjects will be randomly assigned to receive matching placebo tablets containing no toremifene citrate. All treatments will be administered orally once daily for 24 months. An interim analysis of BMD data will be conducted on the first 200 subjects that complete 12 months of treatment and have baseline and 12 month DEXA assessments. The treatment duration of the study will be 24 months. The beginning of study treatment is defined as the first day of toremifene or placebo administration. Subject clinic visits for this study will include the following: screening, randomization, 3, 6, 9, 12, 15, 18, 21, and 24 months. There will be a screening evaluation including procedures that are necessary to determine subject eligibility prior to receiving study treatment. The site will contact the subject by telephone approximately seven days, but no more than ten days, after the randomization visit. The telephone contact will include assessment of study drug compliance and tolerance. Subsequent phone calls will be made at monthly intervals +/- 1 week to assess drug compliance and track serious adverse events. The subject clinic visits will occur every three months for the duration of the study.

**Progress:** This protocol closed enrollment in October 2005, with two subjects enrolled and randomized. Both subjects withdrew and are inactive; no longer being treated or followed. Multiple external adverse events have been submitted. One internal adverse event was reported of dizziness, pain radiating down right arm and unsteady gait, which was assessed as unrelated to study participation (subject had stopped taking study drug three months prior to the event). The protocol remains ongoing pending a formal close-out visit by the study sponsor.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205017	<b>Status:</b> Completed
<b>Title:</b> Madigan Army Medical Center Advanced Laparoscopic Training Using the Pig (Sus scrofa)		
<b>Principal Investigator:</b> LTC Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kenneth S. Azarow, MC; LTC James A. Sebesta, MC; MAJ Alec C. Beekley, MC		
<b>Start - Completion:</b> 10 Nov 2004 - Nov 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 22 Sep 2006

**Study Objective:** Advanced laparoscopic surgical techniques have been developed and are being used with increased frequency. These include techniques upon the stomach especially anti-reflux procedures such as the Nissen fundoplication as well as cholecystectomy and exploring the common bile duct. Laparoscopic techniques for appendectomy, segmental colectomy, total colectomy, colostomy creation, abdominoperineal resection, splenectomy and weight loss surgery have also been developed. The performance of these procedures requires a higher degree of laparoscopic training and skills that must be acquired in the laboratory prior to application in the operating room upon humans. An increased familiarity with these techniques decreases operative time, continues to train staff and residents and minimizes complications for patients while offering state of the art and standard of care surgical services.

**Technical Approach:** To familiarize General Surgery and Urology residents, staff and invited surgeons from our community with techniques in the performance of advance laparoscopic techniques. This training will include esophagus, stomach, biliary, small & large intestine, spleen, liver retroperitoneal and urological procedures. The training benefit will accrue to General Surgery and Urology residents, Staff and invited surgeons by introducing these techniques or reinforcing earlier acquired skills in a controlled environment. Familiarity with these techniques will allow an increased margin of safety for patients, decreased operative time and minimizing of potential complications.

**Progress:** The protocol provided training for 18 medical residents (surgery and urology) in three labs. One lab shared animal resources with protocol #207045 - Duodenal Injury in swine.

### Detail Summary Sheet

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<b>Date:</b> 30 Sep 07	<b>Number:</b> 205040	<b>Status:</b> Completed
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**Title:** The Epidemiology of Nephrolithiasis in Soldiers Returning From Operation Iraqi Freedom

**Principal Investigator:** LTC Karen C. Baker, MC

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**Department:** Surgery/Urology

**Facility:** MAMC

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**Associate Investigator(s):** CPT Jennifer M. Pugliese, MC; CPT Brian J. DeCastro, MC; MAJ Mark I. Anderson, MC; CPT Jack R. Walter, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC; LTC Andrew C. Peterson, MC; LTC Maricela Contreras, MC; Charles G. Beleny, MD

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**Start - Completion:**

11 Feb 2005 - Nov 2008

**Funding:**

DCI

**Periodic Review:**

30 Jan 2006

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**Study Objective:** To study the epidemiology of nephrolithiasis in soldiers returning from Southwestern Asia.

**Technical Approach:** In this four year descriptive, cohort study a database containing demographic, military, medical information will be constructed for soldiers returning from Southwestern Asia who experienced renal colic/nephrolithiasis while deployed. Candidates for the study will be identified by survey during routine post deployment medical screening at the Soldier Readiness Point. Soldiers with a history of urinary calculi or renal colic during their deployment will be referred to the urology clinic evaluation of nephrolithiasis and participation in the database. A CT scan, appropriate serum chemistries, and screening urine test will be performed on all subjects. Investigators hope to better describe the epidemiology of stone disease in soldier deployed in to Southwestern Asia support of Operation Iraqi Freedom and the Global War on Terrorism.

**Progress:** This protocol closed enrollment with six subjects enrolled. Investigators are currently in the final stages of data analysis and writing the publication for submission to a peer-reviewed journal.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205092	<b>Status:</b> Completed
<b>Title:</b> A Multi-center, Randomized Clinical Investigation of Trelstar™ Versus Continued Therapy in Patients Receiving Lupron or Zoladex for Advanced Prostate Cancer		
<b>Principal Investigator:</b> LTC Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC; LTC Andrew C. Peterson, MC		
<b>Start - Completion:</b> 27 Oct 2005 - Jul 2007	<b>Funding:</b> Pharmatech, Inc. via Henry M. Jackson Foundation	<b>Periodic Review:</b> 20 Jul 2006

**Study Objective:** Primary Objective: to compare the inhibitory effect of Trelstar™ versus Lupron or Zoladex on serum testosterone level in patients with advanced prostate cancer. Secondary Objectives: (1) To compare the degree of testosterone suppression by Trelstar™ versus Lupron or Zoladex, (2) To compare the safety and tolerability of Trelstar™ therapy versus Lupron or Zoladex therapy, and

**Technical Approach:** Male patients from the Department of Urology who are currently receiving hormonal therapy for advanced prostate cancer will be offered this research protocol. Subjects will be randomized in a 1:1 ratio to either continuation with current therapy (Lupron or Zoladex) or to study drug (Trelstar), given on a monthly or every three month basis depending on their current treatment schedule. Response will be measured with laboratory tests for testosterone and PSA, and adverse event recording at Baseline and Day 85. Adverse events will be compared with respect to number and severity of events. 95% confidence intervals will be computed for the differences between the Trelstar group and the Continuing therapy group.

**Progress:** This protocol was reported closed by the study sponsor in April 2007, with no subjects screened or enrolled at MAMC.

### Detail Summary Sheet

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<b>Date:</b> 30 Sep 07	<b>Number:</b> 205119	<b>Status:</b> Ongoing
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**Title:** Expression of CXCR4 in Archived Prostate Cancer Specimens and its Association with Patient Demographics, Pathologic Results, and Outcomes

**Principal Investigator:** LTC Karen C. Baker, MC

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**Department:** Surgery/Urology

**Facility:** MAMC

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**Associate Investigator(s):** CPT Brian J. DeCastro, MC; LTC Stephen C. Groo, MC; CPT Joren B. Keylock, MC; CPT Patrick M. McNutt, MS; CPT Jeremy P. Celver, MS; CPT Michael J. Hartenstine, MS; MAJ Garth S. Herbert, MC

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**Start - Completion:**  
15 Aug 2005 - Aug 2007

**Funding:**  
DCI

**Periodic Review:**  
16 Jul 2007

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**Study Objective:** Our primary objective is to compare CXCR4 expression in prostate cancer cells to benign prostate cells in archived prostate specimens. Our secondary objectives are to examine, to the extent possible, the relationships between CXCR4 expression and patient demographics, pathological characteristics, and disease specific outcomes.

**Technical Approach:** This study is a retrospective review of 100-300 patients who underwent radical retropubic prostatectomy or transurethral resection of the prostate. Pathology specimens obtained from previous prostatectomies and transurethral resections of the prostate will be stained for CXCR4 expression with commercially available antibodies and the intensities will be scored using an ordinal scale as judged by three different investigators. The difference in staining of cancerous tissue and benign prostatic tissue will be compared with a t-test and a p value of 5% will be considered statistically significant. These findings will be coordinated with the patients' clinical course located in outpatient records, CHCS, ICDB, and the CPDR. Differences in CXCR4 expression will be compared to demographic factors such as race and age, and the association with disease specific outcomes.

**Progress:** No data has been collected as investigators are still working technical issues related to the staining of the archived tissue.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206039	<b>Status:</b> Completed
<b>Title:</b> SEER Rapid Response Surveillance Study #5, Prostate Cancer Therapy Selection (PCATS) Study		
<b>Principal Investigator:</b> LTC Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Andrew C. Peterson, MC; MAJ Keith J. O'Reilly, MC		
<b>Start - Completion:</b> 5 Jan 2006 - Oct 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8 Dec 2006

**Study Objective:** The objective of the study is to explore way to improve the treatment experience for men living with prostate cancer and their families.

**Technical Approach:** Madigan Army Medical Center will refer patients to Fred Hutchinson Cancer Research Center for participation in this study. Up to 20 MAMC patients who are not too distressed will be approached if they meet eligibility criteria and asked to complete a "consent to contact" form, which will be faxed via confidential line to FHCRC where all other aspects of the study will be conducted. This is a prospective cohort study of adult men with newly diagnosed localized prostate cancer, recruited from urology clinics in the SEER regions (Puget Sound Region: FHCRC, Los Angeles Region: University of Southern California, and the Greater Bay Area Region: Northern California Cancer Center/Kaiser Permanente). The goal is to enroll a total of 850 subjects; 100 from FHCRC, 150 from USC, and 600 from NCCC/KP. There is no coordinating center, as each study site is funded independently and will be completing the study independently. Final data analyses with de-identified data will be pooled and conducted at NCCC/KP.

**Progress:** This protocol was reported as completed by the study sponsor in June 2007. Three MAMC subjects enrolled and completed the study. No results were available at the time of this report.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206072	<b>Status:</b> Completed
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**Title:** A Randomized, Double-Blind, Placebo-Controlled, Multi-Center Phase 3 Study of Denosumab on Prolonging Bone Metastasis-Free Survival in Men with Hormone-Refractory Prostate Cancer

**Principal Investigator:** LTC Karen C. Baker, MC

<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC
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**Associate Investigator(s):** LTC Andrew C. Peterson, MC; LTC Charles G. Henderson, MC; MAJ Michael J. Sebesta, MC; CPT Jennifer M. Pugliese, MC; CPT Dayne M. Nelson, MC; CPT Brian J. DeCastro, MC; MAJ Mark I. Anderson, MC; MAJ Keith J. O'Reilly, MC; COL Robert C. Allen, MC

<b>Start - Completion:</b> 8 Jun 2006 - Mar 2012	<b>Funding:</b> Amgen, Inc. via Geneva Foundation	<b>Periodic Review:</b> 16 Apr 2007
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**Study Objective:** To compare the treatment effect of denosumab with placebo on prolonging bone metastasis-free survival in men with hormone refractory (androgen independent) prostate cancer who have no bone metastasis at baseline.

**Technical Approach:** This is an international, phase 3, randomized, double blind, placebo controlled study in subjects with hormone refractory (androgen independent) prostate cancer. Approximately 1400 subjects will be randomized in a 1:1 ratio to receive denosumab at a dose of 120 mg, SC, Q4W or placebo, SC, Q4W. The randomization schedule will be stratified based on PSA criteria (PSA level  $\leq 8.0$  ng/mL AND PSA doubling time  $\geq 10.0$  months [yes/no]) and previous or current chemotherapy for prostate cancer (yes/no). Subjects will receive investigational product until the end of treatment. The treatment period will end after approximately 660 subjects have developed bone metastasis or died. Subjects will complete the end of study visit approximately 4 weeks after their last dose of investigational product administration. The study duration (excluding the follow up period) is estimated to be 42 months, which includes an enrollment period of approximately 15 months.

**Progress:** This greater than minimal risk study received initial IRB approval 28 March 2006, and final approval was received 8 June 2006. Pre-screening of potential subjects remains ongoing; however, no subjects were enrolled during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206100	<b>Status:</b> Completed
<b>Title:</b> A Randomized, Double-Blind, Multicenter Study of Denosumab Compared with Zoledronic Acid (Zometa®) in the Treatment of Bone Metastases in Men with Hormone-Refractory Prostate Cancer (20050103)		
<b>Principal Investigator:</b> LTC Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Jennifer M. Pugliese, MC; LTC Charles G. Henderson, MC; MAJ Michael J. Sebesta, MC; LTC Andrew C. Peterson, MC; CPT Dayne M. Nelson, MC; CPT Brian J. DeCastro, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC; MAJ Mark I. Anderson, MC		
<b>Start - Completion:</b> 22 Sep 2006 - Jun 2011	<b>Funding:</b> Amgen, Inc. via The Geneva Foundation	<b>Periodic Review:</b> 29 May 2007

**Study Objective:** To determine if denosumab is non-inferior to zoledronic acid (Zometa®) with respect to the first on-study occurrence of a skeletal-related event (SRE) in men with hormone-refractory prostate cancer and bone metastases

**Technical Approach:** This is an international, phase 3, randomized, double-blind, active-controlled study comparing denosumab with zoledronic acid in the treatment of bone metastases in men with hormone-refractory prostate cancer. Approximately 1700 subjects will be randomized in a 1:1 ratio to receive either denosumab, administered at a dose of 120 mg by subcutaneous (SC) injection every 4 weeks (Q4W), or zoledronic acid, administered at a dose of 4 mg (equivalent creatinine clearance-adjusted dose in subjects with baseline creatinine clearance > 60 mL/min) by a single, no less than 15-minute, intravenous (IV) infusion Q4W, in a blinded manner. The randomization will be stratified by previous SRE (yes or no), PSA level (< 10 ng/mL or > 10 ng/mL), and current (defined as within 6 weeks before randomization) chemotherapy for prostate cancer (yes or no). Each subject will receive either an SC injection of denosumab and an IV infusion of zoledronic acid placebo Q4W or an SC injection of denosumab placebo and an IV infusion of zoledronic acid Q4W. Subjects will continue to receive investigational product Q4W until 745 subjects have experienced an SRE (defined as pathological fracture [vertebral or non-vertebral], radiation therapy to bone [including the use of radioisotopes], surgery to bone, or spinal cord compression). Serum denosumab concentration levels will be obtained from a subset of approximately 150 subjects at select centers.

**Progress:** Approved protocol documents were released to the study staff following CRADA/SOW approval 16 October 2006. Multiple external serious adverse event reports reviewed by the PI were submitted to DCI for the file. The consent form was revised per the study sponsor in September 2007 to correct the duration of study participation from 40 months to 16 months. The study remains open to enrollment with no subjects identified as candidates for this trial thus far.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204079	<b>Status:</b> Ongoing
<b>Title:</b> Uniformed Services University Multi-Center National Database for the Center for Prostate Disease Research (CPDR) with Patterns of care, Outcomes, and Prognostic Analyses		
<b>Principal Investigator:</b> MAJ Timothy C. Brand, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Karen C. Baker, MC; MAJ Keith J. O'Reilly, MC; MAJ Keith J. O'Reilly, MC		
<b>Start - Completion:</b> 22 Sep 2004 - Jan 2009	<b>Funding:</b> USUHS via Henry M. Jackson Foundation	<b>Periodic Review:</b> 22 May 2007

**Study Objective:** (1) To collect standardized data on consenting patients treated for prostate disease at specified centers. (2) To maintain an accurate, reliable, secure relational database of patients with prostate disease that meets IRB/HIPPA patient safety, private, and confidentiality guidelines. (3) To coordinate and maintain longitudinal prostate cancer data collection from various sources as a prostate cancer database repository at USUHS. (4) To analyze patterns of care, prognostic factors, quality of life and intermediate and long-term outcomes for prostate cancer and prostate disease entered into this database.

**Technical Approach:** Subjects previously consented in MAMC #98092 will be rolled over into this protocol. Subjects will be asked prospectively to enroll in this database if their doctor recommends that a transrectal ultrasound of the prostate be performed for a medical condition relating to the prostate. Data will be collected and stored in the CPDR database via stand alone data entry. This will include information normally collected on newly diagnosed patients with benign prostatic hypertrophy (BPH) and prostate cancer (CaP) from initial diagnosis to treatment to follow-up care. The development of the CPDR database simply organizes the information into a standard format in order to facilitate the data collection process similar to the hospital tumor registries except that the prostate disease specific information is more comprehensive. Standardized QOL instruments will be employed prior to treatment and periodically during follow-up. The CPDR collaborating statisticians and epidemiologists will be responsible for the quality assessment of the collected data and for the statistical analysis of future research initiatives. The electronic data collected by CPDR will reside in the CPDR National Database and maintained on a secure server at the CPDR Headquarters (part of USUHS) and backed up by the Henry M. Jackson Foundation. The server maintained at CPDR will contain the National Repository for all collaborating sites/locations.

A CPDR research file will be maintained on each subject in locked filing cabinets in the Research Offices of each site. A copy of labs, xrays, bone scans, CT scans, etc., and narrative summaries, operation report(s) related to prostate cancer treatment, radiation therapy summaries, pathology report(s), and death certificates if applicable, will be filed on each patient as well as hard copies of the CPDR forms and the consent form. All sites will use standardized Clinical Research Forms (CRF) which have been designed and can be used as SF600 encounter forms at each patient visit, where permitted. The following data collection forms are used to collect data on all prostate disease patients at participating institutions and are shown and explained in "Forms Manual." (1) Patient Registration, (2) TRUS biopsy, (3) Pre-treatment Staging, (4) Surgery (Radical Prostatectomy), (5) Radical Prostatectomy Pathology, (6) Hormonal Therapy, Chemotherapy and other medications, (7) External Beam Radiation Treatment, (8) Brachytherapy Treatment, (9) Cryotherapy Treatment, (10) Cryotherapy Follow-up, (11) Follow-up, (12) Update of Medical History, (13) CPDR Annual Follow-Up Survey, (14) Necropsy

**Analysis of Data:** The primary purpose of any research database is data analysis to answer research questions and explore hypotheses. With multiple Site Principal Investigators interested



in data analysis, the current system of submitting a CPDR Collaboration consent form will be used. When the study PI, Site PI's or other collaborating researchers want to propose an analysis of multicenter data, a standardized collaboration agreement form will be initiated by the Site PI and his/her CPDR site Research Data Manager. The site personnel will write the proposal in the standardized format and forward it to the Regulatory Affairs Office at CPDR Headquarters. After receiving a CPDR data collaboration request, the Research Opportunity Evaluation Committee at CPDR HQ will discuss the proposal in terms of data availability, statistical support needed, other resources required, military relevance, medical significance and publication probability. If the committee agrees to pursue the proposal and if the request comes from within the CPDR network, the site is asked to prepare the protocol and submit it according to the site's guidelines, while CPDR HQ gets the CPDR collaboration consent from all the sites. Upon receipt of the documentation of approval, CPDR Regulatory Affairs will submit it with a 3204 to USU for approval. Upon receipt of USU approval, the protocol will be forwarded to all contributing sites to prepare and submit to their respective IRB's as required. Approvals will be forwarded to USU REA. If the request comes from outside the CPDR Database network, additional IRB documentation and other appropriate documents specific to the proposal may be requested. These will be submitted to REA with the rest of the submission packet for primary review.

**Progress:** This outcomes database protocol remains open to enrollment, with 93 subjects enrolled at MAMC since the last report for a total of 2,053 subjects since study approval in September 2004. Amendment #3 and a change in the role of PI from Dr. Baker to Dr. Brand were submitted and approved during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 202065	<b>Status:</b> Completed
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**Title:** Oral Ketoconazole For Prevention Of Postoperative Penile Erection, A Prospective, Randomized, Double Blind Trial

**Principal Investigator:** CPT Brian J. DeCastro, MC

<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC
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**Associate Investigator(s):** MAJ Mark I. Anderson, MC; LTC Andrew C. Peterson, MC; CPT Jack R. Walter, MC; MAJ Leah P. McMann, MC; LTC Karen C. Baker, MC; COL Raymond A. Costabile, MC; MAJ Keith J. O'Reilly, MC

<b>Start - Completion:</b> 23 May 2002 - Dec 2002	<b>Funding:</b> DCI	<b>Periodic Review:</b> 25 Apr 2006
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**Study Objective:** To determine if Ketoconazole adequately prevents penile erections after penile surgery.

**Technical Approach:** This study will be broken into three phases. Phase 1-Patients will be identified in the urology clinic scheduled to undergo penile or urethral surgery. Prior to surgery, they will be offered participation and randomized to receive Ketoconazole or placebo. Forty patients will be randomized in a 1:1 ratio to Ketoconazole or placebo. Phase 2-Forty-eight hours before surgery, the patient will be started on the study drug (Ketoconazole 400 mg or placebo TID for a total treatment period of ten days). They will be administered the study questionnaire to fill out at the end of the treatment period. Phase 3- A follow-up telephone call will be made six weeks postoperatively to assess patient satisfaction with the outcome of surgery.

**Progress:** This protocol completed accrual during FY06, with 43 subjects enrolled. Three extra subjects were required in FY07 when two subjects withdrew consent without treatment and one subject had surgery cancelled. The protocol remains ongoing for data analysis of 40 usable data sets.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205136	<b>Status:</b> Ongoing
<b>Title:</b> The Incidence of Infection and Stent Colonization in Patients With and Without Strings		
<b>Principal Investigator:</b> CPT Jennifer L. Gurski, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Dayne M. Nelson, MC; LTC Karen C. Baker, MC; CPT Jennifer M. Pugliese, MC; LTC Andrew C. Peterson, MC; MAJ Mark I. Anderson, MC; MAJ Steven D. Mahlen, MS; MAJ Keith J. O'Reilly, MC; CPT Brian J. DeCastro, MC		
<b>Start - Completion:</b> 5 Jan 2006 - Aug 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 2 Jan 2008

**Study Objective:** To determine if the presence of an external string attached to an indwelling ureteral catheter will lead to an increase in the incidence of infection and stent colonization. To determine which patients are at a higher risk of infection and stent colonization.

**Technical Approach:** This study is a prospective randomized study looking at the infection rate of patients with indwelling ureteral stents. Patients will be randomized to two groups. One group will have nylon strings attached to the stent while the second group will have the strings removed at the time of surgery. Urine samples and stent cultures will be used to determine if there is a significant difference in the infection rate of the two groups. Patient demographics will also be analyzed to see if sex, comorbidities, , duration of stent, or indication for stent placement contributed to an increased rate of significant infection or stent colonization. Significance will be determined using the (X2) test with a p value of < 0.05 being significant

**Progress:** No work was conducted under this protocol during FY07 due to staffing issues. Submission of a change in the role of PI is planned and the study should begin enrollment once IRB approval of the change of PI has been obtained.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207014	<b>Status:</b> Ongoing
<b>Title:</b> Postpartum Durabilities of Anti-Incontinence Surgery in Women of Child-Bearing Age		
<b>Principal Investigator:</b> CPT Jennifer L. Gurski, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Andrew C. Peterson, MC; LTC Jeffery L. Clemons, MC		
<b>Start - Completion:</b> 31 Oct 2006 - 12/09	<b>Funding:</b> DCI	<b>Periodic Review:</b> 13 Nov 2007

**Study Objective:** The objectives of this study are to determine (1) the rate of incontinence surgeries that are performed on women of child-bearing age at Madigan Army Medical Center and (2) the outcomes of bladder suspension/anti-incontinence surgeries in patients of child-bearing age after vaginal or Caesarian section delivery.

**Technical Approach:** This study will be broken into two phases. In phase 1, charts will be pulled from CHCSII and ICDB and reviewed for the aforementioned pre-operative parameters, sling procedures and urethropexies, spontaneous vaginal delivery and caesarian section. In phase 2, all patients identified by the database whose charts were reviewed will be contacted by telephone and a telephonic questionnaire administered by the principal investigator.

**Progress:** This protocol was established because there are so few case reports in the literature of women who have had anti-incontinence surgery and then gone on to have children. No such patients have been identified at MAMC; however, investigators plan to consider expanding the protocol as a multi-institutional study if no patients are identified and enrolled in next 12 months.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205076	<b>Status:</b> Ongoing
<b>Title:</b> Madigan Army Medical Center's Current Clinical Practice and Experience With Osteopenia And Fractures In Men Treated With Androgen Deprivation Therapy		
<b>Principal Investigator:</b> CPT Dayne M. Nelson, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Keith J. O'Reilly, MC; LTC Andrew C. Peterson, MC		
<b>Start - Completion:</b> 6 May 2005 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 28 Aug 2007

**Study Objective:** To determine the incidence of skeletal morbidity and mortality in patients with prostate cancer receiving androgen deprivation therapy at Madigan, as well as the therapies that are currently being prescribed.

**Technical Approach:** This study is a retrospective review of 96 men with prostate cancer currently receiving Androgen Deprivation Therapy (ADT) in the Urology Clinic, specifically looking at the incidence and risk of skeletal morbidity and mortality. In addition, an army wide survey will be conducted with reference to the risks of ADT and the steps army urologists are taking to prevent and treat skeletal morbidity and mortality. The study will record patient demographics, number of months of ADT, incidence and types of fractures occurring after initiation of ADT, results of bone mineral density (BMD) studies conducted after the initiation of ADT, and the types and frequency of treatment prescribed within our facility. The results of the army-wide survey will also be recorded. Data will be analyzed to determine the incidence of bone loss and bone fracture in our patient population currently receiving ADT. The results of the army-wide survey will also be analyzed to determine the awareness of the skeletal morbidity and mortality associated with ADT and what army urologists are doing to monitor, prevent, and treat these effects.

**Progress:** Investigators have reviewed the charts of 96 subjects, and plan to amend the protocol to allow a secondary review of subject records during the next year. This protocol remains ongoing.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 202122	<b>Status:</b> Ongoing
<b>Title:</b> Followup of Testicular Microlithiasis in an Asymptomatic Population		
<b>Principal Investigator:</b> LTC Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Jennifer M. Pugliese, MC; CPT Brian J. DeCastro, MC; COL Raymond A. Costabile, MC; MAJ Leah P. McMann, MC; CPT Frederick L. Stephens II, MC		
<b>Start - Completion:</b> 27 Dec 2002 - Dec 2002	<b>Funding:</b> DCI	<b>Periodic Review:</b> 22 May 2007

**Study Objective:** To determine the incidence of testis tumor at two, five, and ten-year follow-up in the 84 men previously identified with testicular microlithiasis in the original study by Peterson et al. entitled The Prevalence Of Testicular Microlithiasis in an Asymptomatic Screening Population.

**Technical Approach:** Patients will be identified through the data collected at ROTC Advance Camp 2000. All patients identified with TM will be contacted by telephone. If they agree to participate, the study investigator will administer a telephonic questionnaire on year 2002, 2005, and 2010.

**Progress:** Follow up of the original subject population continued during FY07, to screen for the possible development of cancer in this high risk group. Investigators have contacted 63 subjects by phone, e-mail, and mail. One participant has developed testicle cancer since the last follow up.

### Detail Summary Sheet

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<b>Date:</b> 30 Sep 07	<b>Number:</b> 203042	<b>Status:</b> Ongoing
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**Title:** A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study of the Efficacy and Safety of Dutasteride 0.5 mg Administered Orally Once Daily for Four Years to Reduce the Risk of Biopsy-Detectable Prostate Cancer, Protocol Number ARI40006

**Principal Investigator:** LTC Andrew C. Peterson, MC

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**Department:** Surgery/Urology

**Facility:** MAMC

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**Associate Investigator(s):** LTC Karen C. Baker, MC; LTC Charles G. Henderson, MC; MAJ Michael J. Sebesta, MC; CPT Jennifer M. Pugliese, MC; CPT Dayne M. Nelson, MC; MAJ Keith J. O'Reilly, MC; COL Robert C. Allen, MC

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**Start - Completion:**

6 May 2003 - Mar 2007

**Funding:**

GlaxoSmithKline via The Geneva Foundation

**Periodic Review:**

22 Jan 2008

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**Study Objective:** The primary objective of this study is to assess the effect of repeat oral once daily dosing of 0.5mg Dutasteride compared to placebo on the risk of biopsy-detectable carcinoma of the prostate after 2 years and 4 years of treatment.

**Technical Approach:** This is a four-year, international, multicenter, randomized, double-blind, placebo-controlled parallel group study to evaluate the efficacy and safety of oral, once daily dosing 0.5mg of Dutasteride in reducing the risk of biopsy detectable prostate cancer in men with suspicious PSA and an initial negative prostate biopsy who are thereby at increased risk for developing prostate cancer. Approximately 18 patients will be enrolled here at MAMC. Patients will complete a 4 week placebo run-in followed by randomization to either 0.5 mg Dutasteride or placebo in a 1:1 ratio. For up to 4 years, patients will be given a 6 month supply of study medication to self administer. Patients will return to the clinic every 6 months for assessments and a re-supply of medication until study termination. Patients will be contacted by phone 3 months after each clinic visit and 4 months after the final dose of study medication to assess adverse events and concomitant medications. All patients will undergo a TRUS at 2 years and 4 years.

**Progress:** This protocol closed enrollment prior to February 2005, with a total of 16 subjects enrolled. Nine subjects received study treatment; two withdrew from study due to adverse events, seven screen failed, two were discontinued due to disease progression, and five remain on active treatment. One internal adverse event of asymptomatic tachycardia discovered while taking daily blood pressure was reported, and assessed as unrelated to study participation and likely related to the subject's previous known underlying condition. Multiple external serious adverse events were also reported. No changes to the protocol were submitted, except for the addition of an associate investigator.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203081	<b>Status:</b> Completed
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**Title:** Study of the Safety and Effectiveness of the Mentor Two-Piece Inflatable Penile Prosthesis, Protocol Number U108-802-4

**Principal Investigator:** LTC Andrew C. Peterson, MC

<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC
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**Associate Investigator(s):** LTC Karen C. Baker, MC; LTC Charles G. Henderson, MC; MAJ Michael J. Sebesta, MC; CPT Jennifer M. Pugliese, MC; CPT Dayne M. Nelson, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC

<b>Start - Completion:</b> 10 Jul 2003 - Jun 2004	<b>Funding:</b> Mentor via The Geneva Foundation	<b>Periodic Review:</b> 24 Apr 2007
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**Study Objective:** To demonstrate safety and effectiveness of Mentor's Two-Piece Inflatable Penile Prosthesis in men who are undergoing surgical treatment of erectile dysfunction.

**Technical Approach:** This protocol is a multi-center trial. The baseline, pre-operative physical and psychological assessment will serve as a control for each subject. Post-operative measurements of penile erection and psychological assessment should provide a demonstration of the efficacy associated with the penile implants. Patients will have the following baseline study procedures within 30 days of surgery: medical history, physical exam, penile history and measure, psychometric testing with patient satisfaction questionnaire (PSQ), investigators assessment of erectile dysfunction. One or more of the following tests may be used to confirm the diagnosis of erectile dysfunction: Doppler arterial flow, dynamic infusion cavernosometry, rigiscan, and snap-gauge. The operative procedure will take place no more than 30 days after the baseline visit and will record penile measurements and the device catalog number and lot number, anesthesia and other procedure related information. There will be 3 post-operative follow-up evaluations conducted 3-6 weeks after implantation, at 6 months, and 12 months. At each of these follow-ups the following evaluations will be conducted: penile rigidity, adverse event evaluation, urinalysis (12 month follow-up only), patient satisfaction questionnaire (6 and 12 month follow-up only), penile rigidity will be adequate if it is sufficient for sexual intercourse, as determined by the Investigator during postoperative exams and by asking the patient about his ability to perform sexual intercourse. Safety assessment will include: incidence on a per subject basis of all complications (e.g. device malfunctions or infection), time to occurrence of all complications. This study will assess the psychological impact on the subject of implantation of the device. The primary hypothesis will be tested by placing an exact two-sided 95% confidence interval on the re-operation rate. If the upper bound on this confidence interval is less than 0.193 than the null hypothesis will be rejected in favor of non-inferiority to Alpha 1.

**Progress:** This protocol was discontinued per the study sponsor in November 2007, due to patient dissatisfaction. Fifteen subjects consented and eleven subjects completed the study. One subject withdrew without citing a reason; three were dropped from the study (one due to high INR, and no reason given for the other two). None of these three subjects was implanted.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204032	<b>Status:</b> Completed
<b>Title:</b> Prospective, Observational Registry and Patient Survey of the Management of Men with Symptomatic Benign Prostatic Hyperplasia (BPH): BPH Registry and Patient Survey Protocol #L8890		
<b>Principal Investigator:</b> LTC Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Karen C. Baker, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC		
<b>Start - Completion:</b> 5 Apr 2004 - Jan 2005	<b>Funding:</b> Sanofi-Synthelabo, Inc. via The Geneva Foundation	<b>Periodic Review:</b> 2 Mar 2007

**Study Objective:** The aim of the overall registry is to examine the characteristics, management practices, and patient outcomes, including symptom amelioration and disease progression, while exploring the effects of demographic factors, comorbidities, and concomitant medications, in BPH patients in the United States. Safety outcomes, including AEs (common complaints), will also be examined in this patient population.

**Technical Approach:** This is a prospective, multicenter, observational database to collect data on the characteristics, management practices, and subject outcomes of men presenting to their urologist or primary care practitioner with LUTS associated with BPH. It will be offered to a geographically representative group of US physicians who will enroll BPH subjects that are primarily managed conservatively (i.e. watchful waiting or medical intervention). In contrast to a randomized, controlled trial, there are limited predefined interventions and the exclusion criteria are limited. The physician makes his/her own clinical decisions; thus, data captured and reported provide current practice patterns related to diagnosis, management, and results. The registry may also assist physicians in subject follow-up and certain practice management tasks. The data collected will serve to inform the medical community on optimal care. Recently, alpha testing of the registry study was performed at approximately 20 to 30 sites to determine the feasibility of completing the forms (i.e. the burden on subjects and physicians, and the sensitivity to the wording of the sexual questions) during a single visit. Enrollment was competitive with a total of approximately 200 to 300 subjects enrolled. The alpha-testing protocol has provided valuable information that has been used in the design of this protocol for the full-scale registry. The full scale registry is planned to include about 500 sites with approximately 7500 subjects with an option to increase the number of sites, the number of subjects per site, and the registry duration. The primary eligibility criterion is the diagnosis of LUTS associated with BPH at baseline regardless of whether subjects opt for watchful waiting, treatment with 5-alpha-reductase inhibitors or alpha-blockers, or combined medical therapy. Subjects who opt for invasive therapy as an initial treatment or have had surgery in the past for BPH are not eligible for this study. This registry may require minimal additional procedures or interventions as determined by the treating physician. Subjects will be excluded if they decline participation; have concomitant lower urinary tract disease or carcinoma, including history of carcinoma of the prostate or bladder; or have a history of prostatic surgery, including minimally invasive procedures.

**Progress:** This minimal risk protocol was closed out by the study sponsor in June 2007, with fifteen subjects enrolled who completed the study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204078	<b>Status:</b> Completed
<b>Title:</b> Long-Term Open-Label Extension Trial for Subjects Completing the Phase 3 Trial of Fesoterodine (SP584) for the Treatment of Overactive Bladder Syndrome		
<b>Principal Investigator:</b> LTC Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Karen C. Baker, MC; LTC Charles G. Henderson, MC; MAJ Michael J. Sebesta, MC; CPT Jennifer M. Pugliese, MC; CPT Dayne M. Nelson, MC; COL Robert C. Allen, MC; MAJ Leah P. McMann, MC; MAJ Keith J. O'Reilly, MC		
<b>Start - Completion:</b> 24 Aug 2004 - Apr 2005	<b>Funding:</b> Schwarz Biosciences via The Geneva Foundation	<b>Periodic Review:</b> 24 Apr 2007

**Study Objective:** Long-term data on safety, satisfaction and maintenance in subjects taking fesoterodine will be obtained. The subject satisfaction and the treatment benefit of fesoterodine will be assessed.

**Technical Approach:** SP739 is the open-label extension of the double-blind phase 3 trial SP584. Subjects completing the 12 week treatment period in SP584 will have the opportunity to participate in this extension trial. Subjects will be treated from the time of enrollment until fesoterodine becomes commercially available, but no longer than 3 years after enrollment. All subjects will receive 8 mg fesoterodine hydrogen fumarate at the start of the trial. Each subject may request a one time dose reduction to 4 mg fesoterodine hydrogen fumarate after the subject has been on 8 mg fesoterodine hydrogen fumarate for at least 1 month, during a scheduled site visit and upon discussion with the investigator. Such subjects will also be permitted to increase back to 8 mg fesoterodine hydrogen fumarate. This decision can only be made during a scheduled site visit and upon discussion with the investigator. This process can be followed on an annual basis. At a maximum, the number of subjects for this trial will be 810. However, since it is likely that not all subjects treated in SP584 will qualify and choose to enter the long-term open-label extension, it is estimated that at least 450 subjects will be enrolled in SP739.

**Progress:** This protocol was reported as completed in April 2007, with a total of five subjects consented. Of those, one subject completed the study, one withdrew due to reported adverse event of unsteady gait, two withdrew consent, and one was lost to follow-up. Multiple external adverse events were reported. Amendment #2 changes to the protocol and additions to the study staff were submitted and approved during in FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 204086	<b>Status:</b> Completed
<b>Title:</b> Prospective, Open-Label, Non-Comparative, Multi-Center Study to Evaluate the Efficacy and Safety of Ciprofloxacin Extended-Release (Cipro-XR) 1000 mg Tablets Given Once Daily for 7 to 14 Days in the Treatment of Patients 18 Years or Older with Complicated Urinary Tract Infections Caused by Pseudomonas Aeruginosa and Other Common Uropathogens		
<b>Principal Investigator:</b> LTC Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Karen C. Baker, MC; CPT Brian J. DeCastro, MC; LTC Benjamin P. Harrison, MC		
<b>Start - Completion:</b> 17 Sep 2004 - May 2005	<b>Funding:</b> Bayer via The Geneva Foundation	<b>Periodic Review:</b> 27 Jun 2006
<b>Study Objective:</b> To evaluate the safety and efficacy of Cipro XR® 1000 mg PO given once daily for 7-14 days for the treatment of patients with complicated urinary tract infections caused by Pseudomonas aeruginosa and other urinary pathogens. The primary efficacy parameter will be bacteriologic outcome at the Test-of-Cure (Day +5 to +9 post-treatment) visit. Secondarily, clinical response will be assessed at the Test-of-Cure (Day +5 to +9 post-treatment) visit. Clinical cure will be correlated with bacterial eradication in the patient population valid for efficacy. The rate of relapse between the Test-of-Cure visit and the late post-treatment (Day +28 to +42) visit will be determined for patients with complicated UTI caused by P. aeruginosa. The safety of the drug treatment will be monitored. To enroll a minimum of 8 patients with complicated UTI caused by P. aeruginosa that is clinically and microbiologically valid.		
<b>Technical Approach:</b> This is a prospective, open-label, multi-center, Phase IV clinical study to evaluate the efficacy and safety of Cipro XR® 1000 mg PO once daily for 7-14 days for the treatment of patients with complicated UTIs. Patients with clinical signs and symptoms of a complicated UTI that meet all other entry criteria will be treated with Cipro XR® 100 mg PO once daily for a planned treatment course of 7-14 days. Types of diagnoses most likely to be infected with P. Aeruginosa at the time of a complicated UTI include: spinal cord injury/trauma, indwelling urinary catheters (including transurethral and suprapubic), quadriplegia or paraplegia, multiple sclerosis, other risk factors for complicated urinary tract infection and a previous history of a UTI or asymptomatic bacteriuria with P. aeruginosa that was susceptible to flouroquinolones. Patient screening will be performed within 48 hours prior to onset of therapy. During the 7 to 14 day treatment period, there will be an office visit on Day 3-5 of therapy to assess clinical progress. After completion of treatment, there will be a Test-of-Cure (Day +5 to +9 post-treatment) visit for all patients, and for all patients with complicated UTI due to P. aeruginosa, a late follow-up (day +28 to +42 post-treatment) visit to determine the rate of relapse. If, following a full course of therapy, the investigator feels that continued antimicrobial drug therapy is warranted, the patient must be classified as a treatment failure. Before required alternative antimicrobial drugs are given, however, the patient must be fully evaluated and appropriate laboratory tests and cultures performed so that the required information will be available in order to evaluate the study drug.		
<b>Progress:</b> This protocol was reported as completed in June 2007, with a total of five subjects enrolled. Three completed the study, one screen-failed and one withdrew consent due to a need for further antibiotic treatment. One internal adverse event of diarrhea, vomiting, nausea occurred, and two external adverse events were also reported. No updates to the protocol were submitted during FY07.		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205027	<b>Status:</b> Ongoing
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**Title:** A Randomized, Double-Blind, Placebo-Controlled, Multicenter Efficacy and Safety Study of Toremifene Citrate for the Prevention of Prostate Cancer in Men with High Grade Prostatic Intraepithelial Neoplasia (PIN)

**Principal Investigator:** LTC Andrew C. Peterson, MC

<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC
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**Associate Investigator(s):** LTC Karen C. Baker, MC; LTC Charles G. Henderson, MC; MAJ Michael J. Sebesta, MC; CPT Jennifer M. Pugliese, MC; Dieter Kirchheim, MD; CPT Dayne M. Nelson, MC; MAJ Keith J. O'Reilly, MC; COL Robert C. Allen, MC

<b>Start - Completion:</b> 22 Mar 2005 - Feb 2007	<b>Funding:</b> GTx, Inc. via Geneva	<b>Periodic Review:</b> 11 Dec 2007
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**Study Objective:** The primary objective of this study is to assess the efficacy of toremifene in the prevention of prostate cancer in men with high grade prostatic intraepithelial neoplasia (PIN). The Secondary objectives of this study are: (1) To assess the safety of toremifene in men with high grade PIN, (2) To assess the effect of toremifene in high grade PIN, (3) To assess the effect of toremifene on lipid levels, (4) To assess the effect of toremifene on hormone levels, (5) To assess the effect of toremifene on total and % free serum PSA levels, (6) To assess the effect of toremifene on AUA symptom score.

**Technical Approach:** There will be two treatment groups included in this trial. One treatment group will receive tablets containing 20 mg toremifene to be taken daily. The other treatment group will receive matching placebo tablets to be taken daily. Each subject randomized into this study will receive up to 36 months of treatment with a tablet containing 20 mg toremifene or matching placebo tablets. The Screening evaluation includes procedures that are necessary to determine subject eligibility for study treatment. The baseline evaluation is defined as an assessment of subject status prior to any study treatment. If the subject is randomized into this study, the results obtained during the screening and/or randomization visits may be used for the baseline evaluation and comparison with results obtained during or at the completion of the study. Patients will have a 3, 6, 12, 18, 24, 30, and 36 month visits. The primary endpoint will be the diagnosis of prostate cancer through prostate biopsy at 12, 24 or 37 months.

**Progress:** This protocol closed to enrollment with eight subjects enrolled. One subject developed prostate cancer, one subject has been lost to follow up, two subjects withdrew consent and three subjects failed screening. One subject remains active and follow-up will continue until approximately May 2008 for Month 36 visit.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205073	<b>Status:</b> Completed
<b>Title:</b> A Phase 2, Randomized, Multicenter, Placebo-Controlled, Double-Blind Dose-Ranging Clinical Trial to Study the Efficacy and Safety of 5, 15, or 25 mg/day of CyPat™ (Cyproterone Acetate) for the Treatment of Hot Flashes following Surgical or Medical Castration of Prostate Cancer Patients, Protocol #DR-PCA-201		
<b>Principal Investigator:</b> LTC Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Karen C. Baker, MC; LTC Charles G. Henderson, MC; Dieter Kirchheim, MD; MAJ Michael J. Sebesta, MC; CPT Jennifer M. Pugliese, MC; CPT Brian J. DeCastro, MC; CPT Dayne M. Nelson, MC; MAJ Keith J. O'Reilly, MC; COL Robert C. Allen, MC		
<b>Start - Completion:</b> 26 Jul 2005 - Jun 2006	<b>Funding:</b> Duramed via The Geneva Foundation	<b>Periodic Review:</b> 5 Apr 2007
<b>Study Objective:</b> Primary objectives are to compare the efficacy of 5, 15 and 25 mg/day of CyPat™ to placebo when used as "add-on" therapy in reducing the frequency and average severity of moderate to severe hot flashes; to compare the safety of 5, 15 an 25 mg/day CyPat™ to placebo when used as "add-on" therapy; based on the efficacy and safety of each dose, identify the minimally effective dose to be evaluated in a future Phase 3 study. Secondary objectives are to compare the efficacy of 5, 15 and 25 mg/day of CyPat™ to placebo when used as "add-on" therapy in reducing the average severity of all hot flashes and to compare the efficacy of 5, 15 and 25 mg/day of CyPat™ to placebo when used as "add-on" therapy in elimination of all hot flashes.		
<b>Technical Approach:</b> Randomized, double-blind, placebo-controlled 12-week study to compare the efficacy and safety of 5, 15 and 25 mg/day CyPat™ to placebo when used as "add-on" therapy in addition to a stable course of standard pharmacological therapy for prostate cancer in patients with mild to moderate vasomotor symptoms (hot flashes) following surgical or medical castration. A total of 400 patients will be randomized, 100 per treatment arm to achieve 75 analyzable patients per arm. After consenting on the first day of Screening Period, potential patients will hav the following: medical history-including history of hot flashes, physical examination-including assessment of known thromboembolic risk factors, and clinical laboratory evaluations. Once results of the Screening Period evaluations are obtained, those patients thought to be likely to meet the inclusion and none of the exclusion criteria will be invited to participate in a one week single-blind placebo run-in period. Patients must demonstrate at least 21 moderate to severe hot flashes during the 7-day Placebo Run-In Period (this number may be prorated based on the actual duration of the run-in period). Four hundred patients found to meet all the eligibility criteria following the single-blind Placebo Run-In Period will be randomized equally to one of the four double-blind treatment groups: CyPat™ 5, 15 or 25 mg/day or to placebo for a total of 12 weeks. Patients will return for follow-up evaluations each month after beginning double-blind treatment. Patients will maintain a daily paper diary to record the frequency and severity of hot flashes during the treatment period. In addition, a brief physical evaluation will be done, diaries will be reviewed and any adverse events will be recorded at each follow-up evaluation.		
<b>Progress:</b> This protocol was reported by the study sponsor as completed in September 2007. One subject was recruited but failed screening.		

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205079	<b>Status:</b> Ongoing
<b>Title:</b> Microsurgery Training Utilizing The Rat (rattus norvegicus) as a Teaching Model		
<b>Principal Investigator:</b> LTC Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Sean D. Ghidella, MC; LTC John G. DeVine, MC; LTC Paul L. Benfanti, MC; LTC Karen C. Baker, MC; COL Edward D. Arrington, MC; LTC Douglas M. Sorensen, MC; LTC Scott B. Roofe, MC; CPT Dayne M. Nelson, MC; CPT Jennifer L. Gurski, MC; CPT Jennifer M. Pugliese, MC		
<b>Start - Completion:</b> 13 Jul 2005 - May 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 20 Jun 2007

**Study Objective:** The establishment of a microsurgical laboratory utilizing appropriate inanimate materials and anesthetized rats for the teaching and practice of microsurgical techniques will significantly enhance the skills of MAMC surgical staff and residents. It will also correct a deficiency in the Orthopedic Surgery Residency Program (lack of formal micro surgical training) identified by the Residency Review Committee for Orthopedics. Availability of such a laboratory for skill maintenance and enhancement is the standard at teaching institutions that perform microsurgery.

**Technical Approach:** BASIC MICROSURGICAL TECHNIQUES COURSE: This course will consist of five days of progressive microsurgical techniques utilizing didactic or videotape instruction, inanimate "dry labs" for basic instrumentation/orientation training, and practice of prescribed microsurgical procedures utilizing live rats under general anesthesia. The general course flow and animal utilization will be as follows: Day 1: 1) Orientation, course objectives; 2) Basic principles/applications of microsurgery -care and use of surgical microscopes and instruments; 3) Microsurgical instrument lab; 4) Microsuture handling/knot tying/tissue handling; 5) suturing/tissue/handling/"arteriotomy" repair lab with inanimate training materials. Day 2: 1) Rat care and use in microsurgery training; 2) Principles/techniques for end-to-end (ETE) arterial anastomosis; 3) ETE anastomosis-basic technique lab using inanimate training materials; 4) ETE arterial anastomosis lab using live, anesthetized rat. Day 3: 1) Principles/techniques for ETE venous anastomosis. 2) ETE venous anastomosis lab with live, anesthetized rat; 3) Principles/techniques for end-to-side (ETS) arterial anastomosis; 4) ETS arterial anastomosis lab with live, anesthetized rats. Day 4: 1) Principles/techniques for interpositional venous graft; 2) Interpositional venous graft lab with live, anesthetized rats; 3) Principles/techniques for neurorrhaphy; 4) neurorrhaphy lab with live, anesthetized rats. Day 5: 1) Specialty-specific instruction/laboratory with live, anesthetized rats; 2) Vasovasostomy. 3) Fallopian tube anastomosis; 4) Micro-tendon repair; 5) Free vascular tissue transfer; 6) Course Summary/Review/Critique.

**UROGENITAL (OB/GYN, UROLOGY) MICROSURGERY TRAINING:** This course will consist of two (2) consecutive, eight (8) hour days of training in the instrumentation, principles and performance of common urogenital microsurgery techniques and procedures. Course content will generally, but not necessarily follow the detailed synopsis below. Day 1: Introduction to microsurgery (video, slides, written materials, discussion). Day 2: Principles of urogenital surgical site assessment and repair (video, slides, written materials, discussion).

**ADVANCED MICROSURGERY TECHNIQUES (AMT) COURSE:** Advanced microsurgery courses will consist of five (5) consecutive, eight (8) hour training days. Participants in advanced microsurgery training course will plan their proposed advanced procedures with the course instructor(s) prior to course commencement. Course instructors will confer with the DCI Veterinarian regarding proposed advanced procedures and animal species preferences at least 30

days prior to course commencement, in order to ensure adequate consideration for animal availability, care and postoperative well being. Advanced procedures may consist of techniques such as limb/digit replantation, free vascularized soft tissue or bone grafts, advance neurologic or urogenital reconstructions, anatomical augmentation, organ transplantation, etc. NOTE: Because of the variety of subspecialty-specific procedures to be considered for AMT training, it is not feasible to list or describe specific procedures in this protocol. AMT course schedules and proposed procedures will require MAMC IACUC approval PRIOR to course commencement. Training coordinators for AMT courses will provide reasonable description of the proposed procedures, in writing and will discuss potential procedure-specific post-operative complications for consideration during IACUC review of proposed AMT course schedules.

Day 1: Introduction to microsurgery (video, slides, written materials, discussion) Instrumentation and instrument handling, suture and supplies, suture manipulation and knot tying (video, slides, written materials, discussion) Proper use of the surgical microscope and surgical loupes, suture manipulation and knot tying (laboratory exercise; inanimate training materials) Procedures for end-to-end (ETE), end-to-side (ETS), and side-to-side (STS) anastomosis of tubular organs, and longitudinal defect repair (video, slides, written materials, discussion- Practice ETE, ETS, and STS tubular anastomoses, and longitudinal defect repair (laboratory exercise; inanimate training materials or rat cadaver). Day 2: Principles of urogenital surgical site assessment and repair (video, slides, written materials, discussion) Preparation and suturing techniques for fallopian tube or vas deferens repair/reconstruction (video, slides, written materials, discussion. Practice fallopian tube or vas deferens repair/reconstruction techniques using rat uterus and femoral artery/vein, with surgical loupes and microscope (laboratory exercise; anesthetized rat) Elective instrumentation/procedures laboratory session (e.g. continuation of tubal/vas deferens reconstruction/repair techniques; ureteral injury repair techniques; basic microvascular, microneural, microlymphatic repair techniques; urogenital applications of the non-penetrating Vascular Closure System- VCS, US Surgical Inc. etc) (laboratory exercise; inanimate tissue or anesthetized rat)

#### ADVANCED MICROSURGERY TECHNIQUES (AMT) COURSE:

Advanced microsurgery courses will consist of five (5) consecutive, eight (8) hour training days. Participants in advanced microsurgery training course will plan their proposed advanced procedures with the course instructor(s) prior to course commencement. Course instructors will confer with the CIF veterinarian regarding proposed advanced procedures and animal species preferences at least 30 days prior to course commencement, in order to ensure adequate consideration for animal availability, care, and postoperative well being. /advanced procedures may consist of techniques such as limb/digit replantation, free vascularized soft tissue or bone grafts, advance neurologic or urogenital reconstructions, anatomical augmentation, organ transplantation, etc. Note: Because of the variety of sub-specialty specific procedures to be considered for AMT training, it is not feasible to list or describe specific procedures in this protocol. AMT course schedules and proposed procedures will require 60 MDG IACUC approval PRIOR to course commencement. Training coordinators for AMT courses will provide reasonable description of the proposed procedures, in writing, and will discuss potential procedure-specific postoperative complications for consideration during IACUC review of proposed AMT course schedules. Day 1: Review of microsurgery principles and techniques (video, slides, written materials, discussion. Presentations/discussion of first proposed advanced procedures, including postoperative management/monitoring issues, etc. (video, slides, written materials, discussion. Practice first advance procedures-terminal /non-survival; instructor evaluation of participant technical proficiencies (laboratory exercise; anesthetized rat, rabbit, pig, sheep/goat terminal/non-survival. Day 2: Perform advance procedures described on Day 1, morning and practiced Day 1, afternoon; recovery of anesthetized animal (laboratory exercise; anesthetized rat, rabbit, pig, sheep/goat. Postoperative assessment of morning surgery animal/operative site; presentations/discussion of second proposed advanced procedures, including postoperative management/monitoring issues, etc. (video, slides, written materials, discussion. Day 3: Assessment of Day 2 animal/operative site;

perform advanced procedures described Day 2 afternoon on new animal; recovery of anesthetized animal (laboratory exercise; anesthetized rat, rabbit, pig, sheep/goat. Presentations/discussions of third proposed advance procedure, including postoperative management/monitoring issues, etc.; Postoperative assessment of morning surgery animal/operative site, and Day 2 animal /operative site (video, slides, written materials, discussion); Day 4: Assessment of Day 2 & 3 animals/operative sites; perform advanced procedures; Presentations/discussion of fourth proposed advanced procedures, including postoperative management/monitoring issues, etc.; postoperative assessment of Day 3 animal/operative site (video, slides, written materials, discussion); Day 5: Assessment of Day 3 animal/operative site; perform advanced procedures animal- terminal/non-survival procedure (laboratory exercise; anesthetized rat, rabbit, pig, sheep/goat, terminal/non-survival).

**Progress:** This protocol provided microsurgical and vascular surgery training for 10 medical residents in two training labs.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205135	<b>Status:</b> Ongoing
<b>Title:</b> Acute Urinary Retention and the Role of Fill and Pull Voiding Trials		
<b>Principal Investigator:</b> LTC Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Brian J. DeCastro, MC; CPT Jennifer M. Pugliese, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC; LTC Karen C. Baker, MC; MAJ Mark I. Anderson, MC; CPT Dayne M. Nelson, MC		
<b>Start - Completion:</b> 5 Jan 2006 - Sep 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 23 Oct 2007

**Study Objective:** Define the role of fill and pull voiding trials versus simple catheter removal in men with acute urinary retention.

**Technical Approach:** This is a prospective randomized study of 100 patients who present to the Urology clinic with acute urinary retention. These patients have or will have a Foley catheter placed to drain their bladder on presentation. Initial evaluation will include urinalysis, urine culture, and routine serum studies. Patients will be started on tamsulosin if not contraindicated or already on alpha-blocker therapy. Those already on alpha-blockers will continue the original therapy. Patients will follow-up with the urology service for catheter removal on day 5-7. Patients will have complete history and physical examination and be randomized to fill and pull voiding trial or catheter removal following consent. Fifty patients will be included in each arm of the study. Patients will have a transrectal ultrasound to size prostate at time of catheter removal. If patients pass voiding trial they will have a follow-up visit at 1 month to assess voiding symptoms. If patients fail voiding trial they will continue with catheter drainage for an additional 5-7 days and have the same method of catheter removal. If patients have success they will have the above follow-up. If patients fail the voiding trial for a second time, they will undergo urodynamics and be managed by current standards of care. Data recorded will include; the cause of retention, American Urologic Association symptom and bother score, serum creatinine, prostate serum antigen (PSA), urine analysis and culture results, prostate size, outcome of voiding trial, and 3 month follow up data.

**Progress:** A total of five subjects enrolled in this study. Several people have been referred for urinary retention, but were not interested in the study or were excluded. Subject enrollment continues.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206031	<b>Status:</b> Ongoing
<b>Title:</b> Adult Circumcision: Template vs Standard Sleeve Technique		
<b>Principal Investigator:</b> LTC Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Karen C. Baker, MC; CPT Jennifer M. Pugliese, MC; CPT Dayne M. Nelson, MC; MAJ Mark I. Anderson, MC; CPT Brian J. DeCastro, MC		
<b>Start - Completion:</b> 22 Feb 2006 - Jan 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 11 Dec 2007

**Study Objective:** To compare the Adult template circumcision with the standard sleeve technique.

**Technical Approach:** This study is a prospective randomized study comparing the standard sleeve technique (current standard) with the Adult template circumcision technique. Patients will be randomized to two groups containing 50 patients each. An interim analysis will be done at 50 patients. The two groups will be compared by operative times, blood loss, complication rates, and overall patient satisfaction as assessed by the attached patient satisfaction form. Significance will be determined using the (X2) test with a p value of < 0.05 being significant.

**Progress:** Thirteen subjects enrolled in this study at MAMC, eleven during FY07. One adverse event has been reported (scar tissue requiring surgical repair). Study enrollment continues.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 206102	<b>Status:</b> Completed
<b>Title:</b> Phase 2 multicentre, randomised, double-blind, placebo-controlled, pilot study to determine proof of efficacy, safety, tolerability and pharmacokinetics of intravesical PSD597 in the symptomatic management of interstitial cystitis/ Painful bladder syndrome (IC/PBS)			
<b>Principal Investigator:</b> LTC Andrew C. Peterson, MC			
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Karen C. Baker, MC; LTC Charles G. Henderson, MC; MAJ Michael J. Sebesta, MC; CPT Jennifer M. Pugliese, MC; CPT Dayne M. Nelson, MC			
<b>Start - Completion:</b> 13 Sep 2006 - Dec 2006	<b>Funding:</b> Plethora Solutions Ltd via The Geneva Foundation	<b>Periodic Review:</b> 26 Jun 2007	
<b>Study Objective:</b> Primary Objective: To assess the percentage of patients who respond to PSD597, assessed as "moderately improved" or "markedly improved" measured by a Global Response Assessment (GRA), compared to placebo, at day 15 following a 5-consecutive day course of treatment.  Secondary Objectives: (1) To assess changes in GRA measured by a 7-point scale, (2) to assess changes in bladder pain measured by 10-point Likert scale, (3) to assess changes in frequency measured by a voiding log, (4) to assess changes in urgency measured by 10-point Likert scale, (5) to assess changes in symptoms and problems associated with interstitial cystitis measured by the O'Leary Sant Interstitial Cystitis symptom and problem indexes (6) to assess the safety and tolerability of PSD597 instilled into the bladder and (7) to characterize the pharmacokinetics of single and multiple doses of intravesical PSD597 in a sub-group of patients.  <b>Technical Approach:</b> This is a phase II, multicenter, randomized, double-blind, placebo-controlled, parallel group, pilot study to determine proof of efficacy, safety, tolerability and pharmacokinetics of intravesical PSD597 in the symptomatic management of IC/PBS. 100 subjects with a clinical diagnosis of IC/PBS with symptoms persisting for at least three months prior to study entry and including pain of bladder origin will be enrolled into the study. Following consent subjects will undergo screening procedures in the clinic within 14 days prior to baseline (day 1). At baseline (day 1), all eligible subjects will be randomly allocated (1:1) to treatment with PSD597 or placebo. Double-blind treatment will be given as a daily instillation for five consecutive days (Monday - Friday, days 1 - 5), to be administered in hospital as an outpatient. Following double-blind treatment, all subjects will attend clinic for follow-up evaluations on days 8 and 15. All subjects will then be offered the option of open-label treatment with PSD597 for five further days (Monday - Friday, days 15 - 19) - administered in hospital as an outpatient. All subjects, whether or not they opt to receive open-label treatment, will attend clinic for further final follow-up evaluations on days 22 and 29.  <b>Progress:</b> This protocol was completed at MAMC during FY07. Approved protocol documents were released to the study staff following CRADA/SOW and Amendment #2 approval in October 2006. Changes to the protocol included an increase in the number of subjects to be enrolled from 5 to 15 to account for subjects that consent, but subsequently screen fail. A memo was submitted 16 October 2007, announcing closure of the protocol at MAMC with four subjects consented. Two subjects withdrew consent; the first was due to childcare issues and time constraints, and the second subject wanted to receive active study drug in Canada. One subject screen failed and one subject completed the study. A list of protocol deviations discovered at time of study closeout was included in the final report to the IRB. No external or internal adverse events were reported while the study was active at MAMC.			

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206117	<b>Status:</b> Ongoing
<b>Title:</b> Comparison of Non-Contrast Abdominal Computed Tomography (CT) to Contrast CT, Intravenous Pyelography (IVP) and Nuclear Renal Scan for Determination of Renal Function: A Retrospective Review		
<b>Principal Investigator:</b> LTC Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Jennifer L. Gurski, MC		
<b>Start - Completion:</b> 15 Aug 2006 - Sep 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** Objective is to establish the ability of non-contrast CT ("stone protocol CT") to determine renal function without the use of intravenous contrast or radio-pharmaceutical (IVP, contrast CT, or nuclear renal scan).

**Technical Approach:** The CHCS database will be reviewed for patients who have undergone non-contrast CT scanning of the abdomen for any diagnosis. Patients who have undergone subsequent functional studies in addition to the non-contrast study will be included in the study. A multivariate analysis will be performed to determine if non-contrast CT scanning can be used to estimate renal function without the use of contrast agents or radio-pharmaceuticals.

**Progress:** Investigators have reviewed the 200 charts requested, and plan to submit an amendment to the protocol requesting approval to search for additional charts meeting the inclusion criteria. Analysis of the CT scans for measurements will continue during FY08.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205088	<b>Status:</b> Terminated
<b>Title:</b> The Value of Resistive Index: A Longitudinal Study of Confounding Variables and Their Impact - A Pilot Study		
<b>Principal Investigator:</b> CPT Jennifer M. Pugliese, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD; LTC Benjamin W. Starnes, MC; CPT Jason T. Perry, MC		
<b>Start - Completion:</b> 24 May 2005 - Dec 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 10 May 2006

**Study Objective:** To determine the course and variability of resistive index as measured by Doppler ultrasound in patients with new onset hypertension over time as their disease progresses and new medications are added.

**Technical Approach:** In this prospective, observational study, a database containing demographic and medical information will be constructed for patients with newly diagnosed hypertension. Candidates for the study will be identified by their primary care providers and referred to the vascular surgery clinic for consideration for the study. A baseline Doppler ultrasound and resistive index calculation will be performed at that point prior to the initiation of any medical therapy for their hypertension. A group of healthy volunteers will also receive a Doppler ultrasound measured resistive index calculation as a control group. Doppler ultrasound and resistive index calculations will then be undertaken at three month intervals in the study patients as well as in the control group. We hope to better determine the utility and accuracy of resistive index in diagnosing renal artery stenosis and determining which patients would benefit from surgical intervention based on the information obtained from this study.

**Progress:** No work was conducted under this study during FY07, and no subjects enrolled since initial IRB approval in May 2005, so investigators decided to terminate the project.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207005	<b>Status:</b> Ongoing
<b>Title:</b> The Identification of Seminal Plasma Protein Biomarkers in Patients Presenting with Infertility, Hydrocele, Varicocele, Spermatocele and Testicular Masses		
<b>Principal Investigator:</b> CPT Jennifer M. Pugliese, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Karen C. Baker, MC; CPT Michael J. Hartenstine, MS; Danielle L. Ippolito, PhD		
<b>Start - Completion:</b> 20 Oct 2006 - Oct 2009	<b>Funding:</b> DCI	<b>Periodic Review:</b> 11 Oct 2007

**Study Objective:** The objective of this study is to determine if specific, unique protein biomarkers exist in seminal plasma that may be used in the diagnosis or treatment of patients presenting to the urology clinic with infertility, hydrocele, varicocele and testicular masses.

**Technical Approach:** A pilot study will be conducted using 5 normal controls in order to delineate which methods and proteomic chips are necessary for the analysis of the specimens. Normal controls will be recruited from the Urology clinic to provide two semen samples. The first sample will be sent to the Madigan laboratory for analysis in order to rule out any underlying, previously unidentified abnormalities. If no exclusion criteria are identified, a second sample will be obtained, processed by the main investigator in the Urology clinic and used for study analysis. Those control candidates who are found to have abnormal semen parameters on the initial semen analysis will be informed of the results and managed accordingly. Once the pilot study has been completed, the study populations will be recruited.

Patients presenting to the Urology clinic for routine evaluation of infertility will undergo urologic evaluation; history and directed physical exam. Two semen analyses will be obtained through the Madigan laboratory. Patients will be recruited for study analysis if both semen analyses show oligospermia, asthenospermia, oligoasthenospermia or azospermia. Informed consent will be obtained and the patient will provide a semen sample for analysis, which will be processed by an investigator in the Urology clinic. Evaluation and treatment of infertility will proceed within the standard of care.

This process will be repeated for patients presenting to the Urology clinic for the evaluation of hydrocele, varicocele, and solid testicular mass. From these study populations, patient samples will be divided into several groups. Of the infertility patient samples, group 1 will include oligospermic samples and group 2 will include azospermic samples. Oligospermic samples will include those samples that demonstrate oligoasthenospermia, oligoteratospermia and oligoasthenoteratospermia. Hydrocele patients, varicocele patients and solid testicular mass patients will comprise three separate groups. Proteomic profiles on select subgroups will be collected using surface enhanced laser desorption time of flight mass spectroscopy (SELDI-TOF). Initially, seminal plasma will be profiled neat on various chromatographic chip surfaces. After assessing the effectiveness and informativeness of profiling neat samples, selected chromatographic surfaces will be used for additional profiling or consideration will be given to the need for additional fractionation of plasma samples prior to SELDI analysis. Seminal plasma from the control group will be profiled separately to establish baseline values and sample to sample variability in spectral protein peaks. At the time of analysis, sufficient control group samples will be pooled to create a standard reference sample to be included with all future SELDI analysis'.

**Progress:** This minimal risk protocol received approval by the Expedited Review Committee 20 October 2006. Five subjects enrolled during FY07. Investigators continue to screen eligible subjects.

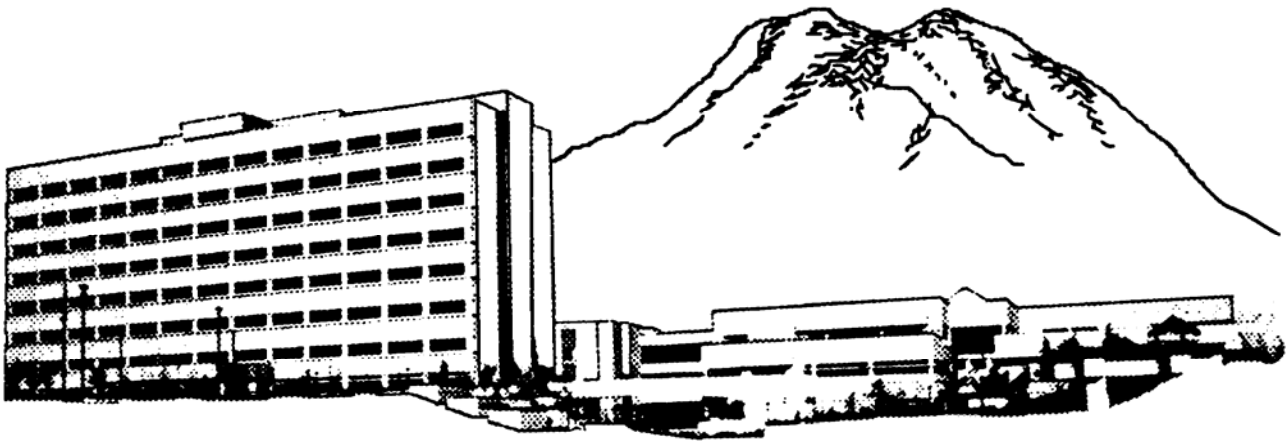
### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207065	<b>Status:</b> Ongoing
<b>Title:</b> The Role of Extended Meatoplasty in the Management of Urethral Stricture Disease Due to Lichen Sclerosus		
<b>Principal Investigator:</b> CPT Jennifer M. Pugliese, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Andrew C. Peterson, MC		
<b>Start - Completion:</b> 27 Feb 2007 - Feb 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to define the utility and outcomes of extended meatoplasty in the treatment of distal urethral strictures in patients with lichen sclerosus.

**Technical Approach:** A retrospective chart review and telephonic post-operative follow-up questionnaire will be conducted to attempt to further define the role of extended meatoplasty in the surgical management of male urethral stricture disease due to lichen sclerosus. This minimally invasive surgical technique may then become more widely used in the urologic community as a tool which may aid in the resolution of lichen sclerosus and the prevention of squamous cell carcinoma of the penis and urethra.

**Progress:** This minimal risk protocol received initial approval by the Expedited Review Committee on 27 February 2007. A total of 26 subject charts have been reviewed and questionnaires completed. Data collection and analysis is still ongoing.



## **Detail Summary Sheets**

Vascular Surgery, Department of Surgery



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 202086	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized, Controlled Multicenter Trial of Vacuum Assisted Closure Therapy™ in the Treatment and Blinded Evaluation of Diabetic Foot Ulcers (Protocol VAC2001-08)		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Monica H. Schweinberger, DPM; Vickie R. Driver, DPM; Gary P. Degen, DPM		
<b>Start - Completion:</b> 24 Sep 2002 - Aug 2005	<b>Funding:</b> KCI USA via The Geneva Foundation	<b>Periodic Review:</b> 29 May 2007

**Study Objective:** The primary objectives are to determine the incidence of complete ulcer closure, accelerated ulcer closure or facilitation of surgical closure, and change in ulcer area. The secondary objectives are to determine the reduction in complications, including amputations, quality of life, and average total cost of care.

**Technical Approach:** This study will be looking at approximately 18 male or female patients, 18 years of age or older that have diabetic foot ulcers > 2cm<sup>2</sup> in area after debridement. Visit #1- Eligible patients will be given a physical exam, a relevant medical and surgical history will be taken, concomitant medications will be listed, and blood drawn for laboratory tests and the patient will be given a Quality of Life Questionnaire to complete. Visit #2, the patient will be randomized and given their first treatment. At subsequent visits the study group patients will have medical and medication histories updated, digital photographs will be taken of the wound, measurements taken, dressing applied and instructions on continued care given. The control group will receive standard of care treatment. All patients will receive off-loading therapy preventatively and therapeutically as indicated. Off-loading therapy is used to keep pressure away from the wound area by means of the use of a special shoe, boot, cane, or, in some cases, a wheelchair. No patient will remain in the study for longer than 12 months (total duration). The wound will be examined for recurrence or determination of ulcer status.

**Progress:** This protocol closed enrollment in March 2006, with fourteen subjects enrolled, but remained ongoing during FY07 pending formal study close-out by the sponsor, KCI. Nine subjects completed the trial, two withdrew consent, two were dropped on the advice of the principal investigator, one screen failed, and one was lost to follow-up. Eighteen external adverse events were reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 203055	<b>Status:</b> Completed
<b>Title:</b> A Randomized, Controlled, Multicenter Trial of Vacuum Assisted Closure Therapy™ in the Treatment and Blinded Evaluation of Pressure Ulcers, Protocol Number VAC2001-01		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Benjamin W. Starnes, MC; Mary Anne Landowski, MSN, RN		
<b>Start - Completion:</b> 16 May 2003 - May 2004	<b>Funding:</b> KCI USA via The Geneva Foundation	<b>Periodic Review:</b> 26 Jan 2007

**Study Objective:** The primary objective of this study is to determine if topical negative pressure therapy delivered by the Vacuum Assisted Closure device is clinically efficacious and cost effective in the treatment of pressure ulcers.

**Technical Approach:** The study will look at 10 males or females, 18 years or older, who have the presence of Stage III or Stage IV pressure ulcers located on the trunk or trochanter region. At Visit 1, the patient will have a relevant medical and surgical history taken; physical exam with height and weight; concomitant medications recorded; blood drawn for lab tests. Visit 2 takes place 7days after visit 1 -debridement and assignment to study or control groups will be done with a 1:1 ratio. Study group will have the V.A.C. therapy; Control group will receive standard of care treatment. Pain assessments are completed; data collected; digital photography; bi-layer tracing of the wound will be measured; Granulation tissue formation will be categorically estimated in % and recorded; wound assessment; Quantitative/Semi-Quantitative Bacterial Cultures performed; Patient will complete the wound pain assessment. The VAS pain assessment will be done 1/2 hour prior and post the wound dressing changes. Visits 3 through 7 (+/- 2 days) and 8 (+/- 7 days) - All patients are placed on appropriate Group II or Group III bed surface; wound examinations and assessments will be done: The same ulcer documentation will be done as in Visit 2 above, plus the Interim dressing changes will be documented, i.e. average number of interim dressing changes calculated per day and per week; a list of materials used are recorded; the occupation of the person performing the dressing changes will be recorded. Visit 9 will be the first long term follow-up assessment of recurrence. Visit 10 will be the second long term follow-up/End of Study visit. No patient will remain on the study longer than 12 months (total study duration). The ulcer will be examined for recurrence or determination of ulcer status and a VAS pain assessment will be completed 1/2 hour before and 1/2 hour after the wound dressing changes.

**Progress:** The study sponsor closed this protocol in February 2007, with two MAMC subjects enrolled, randomized and completed the study. One subject failed screening. Multiple external adverse events were reported during FY07.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205010	<b>Status:</b> Completed
<b>Title:</b> Linezolid In The Treatment Of Subjects With Complicated Skin And Soft Tissue Infections Proven To Be Due To Methicillin-Resistant Staphylococcus Aureus		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Monica H. Schweinberger, DPM; LTC Benjamin W. Starnes, MC; Vickie R. Driver, DPM; Gary P. Degen, DPM		
<b>Start - Completion:</b> 3 Mar 2005 - Sep 2005	<b>Funding:</b> Pfizer via The Geneva Foundation	<b>Periodic Review:</b> 24 Oct 2006

**Study Objective:** Primary Objective: To compare the clinical efficacy of linezolid to vancomycin in the treatment of complicated skin and soft tissue infections (cSSTI) due to MRSA in adult subjects at the End of Study (EOS) visit. Secondary Objectives: (1) To compare the clinical efficacy, and safety and tolerability of linezolid to vancomycin in the treatment of cSSTI due to MRSA in adult subjects at the End of Treatment (EOT) visit. (2) To compare the bacteriological efficacy, and safety and tolerability of linezolid to vancomycin in the treatment of cSSTI due to MRSA in adult subjects at the EOT and the EOS visits. (3) To compare the medical resource utilization of linezolid and vancomycin for this subject population.

**Technical Approach:** This is a Phase IV, multicenter, randomized, open-label, trial with two treatment groups, linezolid IV or oral tablets and vancomycin IV infusion, to be administered for a planned duration of 7-14 days of treatment. Subjects with documented MRSA bacteremia may be treated up to 21 days at the discretion of the investigator. Subjects will be randomly assigned to receive either linezolid intravenous (IV) infusion or oral tablets 600 mg every 12 hours or vancomycin intravenous (IV) infusion 15mg/kg per dose every 12 hours in subjects with normal renal function. Dosage and interval should be adjusted based on standard nomograms according to renal function. Vancomycin levels should be performed at the investigator's discretion. Aztreonam intravenous (IV) infusion 1-2 grams every 12 hours may also be administered as required for suspected or proven Gram-negative pathogens until culture results are obtained. If the subject does not have a Gram-negative pathogen, aztreonam will be discontinued, at the discretion of the investigator. An alternative agent may be substituted for aztreonam if the local susceptibility patterns preclude its use or for other reasons the subject may be unable to use it. The agent selected must not have activity against MRSA. Metronidazole intravenous (IV) infusion or oral tablets 500 mg every 8 hours may also be administered as required for suspected or proven anaerobic pathogens until culture results are obtained. If the subject does not have an anaerobic pathogen, metronidazole will be discontinued at the discretion of the investigator. Approximately 600 subjects per arm will need to be enrolled for a total sample size of 1200 subjects. There is no planned formal interim analysis.

**Progress:** This protocol was reported as completed September 2007, with eight subjects enrolled. Six subjects completed the study, but one subject was unable to complete the follow-up clinic visits per protocol due to VA insurance issues. One subject died of cardiac arrest, which the PI assessed as related to existing medical conditions and unrelated to study participation. Several external adverse event reports were also submitted.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 205091	<b>Status:</b> Ongoing
<b>Title:</b> The Prevalence and Progression of Carotid Artery Stenosis in Patients Undergoing Radiation for Head and Neck Cancer		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Garth S. Herbert, MC; MAJ Joseph P. Brooks, MC; LTC Douglas M. Sorensen, MC; COL John B. Halligan, MC; CPT Michael J. Wilhelm, MC; Billinda Tatum, RN, CCRC; LTC Benjamin W. Starnes, MC		
<b>Start - Completion:</b> 16 Jun 2005 - Feb 2015	<b>Funding:</b> DCI	<b>Periodic Review:</b> 29 May 2007

**Study Objective:** (1) To establish the prevalence of carotid artery stenosis and its risk factors in patients with head and neck cancer. (2) To establish the course of progression of carotid artery stenosis in patients undergoing radiation for head and neck cancer. (3) To determine the correlation (if any) of C-reactive protein levels with carotid artery disease in patients undergoing radiation for head and neck cancer.

**Technical Approach:** This is a prospective cohort study. The screening tests are already being offered by the Vascular Surgery Service at MAMC. Eligible patients would be consented and their name, age, social security number, and other demographic data recorded in the ICDB and flagged as a study participant. A short screening questionnaire (recorded in the initial ICDB note) designed to identify other risk factors for or symptoms of carotid artery stenosis will be completed at this time.

Patients referred to the Vascular Surgery Clinic at MAMC would have a screening carotid duplex performed within one month of the initiation of XRT in order to establish the baseline level of disease present in these patients. Each patient will also be asked to complete a questionnaire to determine risk factors for and previous symptoms of vascular disease. The resultant data from each duplex will be recorded in the patient's chart maintained at the vascular surgery clinic, and the questionnaire will be kept in the chart as well. After performance of the carotid ultrasound, the patient will be sent to the lab for blood draw to determine a baseline C-reactive protein level. After radiation therapy, the dose of radiation administered to each carotid artery will be recorded. If a hemodynamically significant stenosis is identified, the patient would be evaluated for a carotid endarterectomy by ACAS and NASCET criteria, as is the standard of care in the Vascular Surgery Clinic at MAMC.

After the initial screening, the patients will undergo follow-up carotid duplexes every six months in order to define the progression of carotid artery disease following radiation therapy. As with the initial duplex, any patient with a hemodynamically significant abnormality on follow up studies would be evaluated for a carotid endarterectomy by ACAS and NASCET criteria. After the screening, positive results requiring further diagnostic evaluation would be compiled and follow-up would be arranged for definitive testing and subsequent risk factor modification and/or intervention. These subjects will be identified as members of the "high risk" subgroup in terms of future stroke potential to their primary care provider. Patients who agree to additional blood draws will also have a C-reactive protein level determined on the same day the follow-up carotid duplex is performed.

**Progress:** Previously enrolled subjects continue to undergo serial duplex examinations. Recruitment of eligible subjects has slowed due to manpower limitations in the ENT clinic. Investigators are looking into additional nursing support to permit improved recruitment of all eligible subjects in the future.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206012	<b>Status:</b> Terminated
<b>Title:</b> A Comparative Prospective, Randomized, Double-Masked, Parallel Group, Sham-Controlled Trial of MIST Therapy for the Reduction of Pain in Chronic Lower Extremity Ulcers		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Mary Anne Landowski, MSN, RN; LTC Benjamin W. Starnes, MC; Monica H. Schweinberger, DPM; Leslie B. Schoneman, PA-C; Gary P. Degen, DPM; Vickie R. Driver, DPM; Thomas S. Roukis, DPM		
<b>Start - Completion:</b> 17 Jan 2006 - Apr 2006	<b>Funding:</b> Celleration, Inc. via Geneva Foundation	<b>Periodic Review:</b> 18 Oct 2006
<p><b>Study Objective:</b> Primary Objectives: Effectiveness (1) to assess the reduction in baseline numeric pain rating scale scores comparing MIST Therapy in relation to sham control through treatment week 4. Safety: (2) to compare the incidence of adverse events among patients receiving MIST Therapy in relation to the sham control treatment group. Secondary Objectives: (1) to compare the use of analgesic medication between the two treatment groups through treatment week 4 and (2) to compare the quality of life scores using an SF-12v2 scale between the two treatment groups through treatment week 4.</p> <p><b>Technical Approach:</b> The trial is designed as a comparative, prospective, randomized, double-masked, parallel group, controlled, multi-center study of patients presenting with chronic non-healing lower extremity venous insufficiency, arterial or sickle cell ulcers. To be eligible for randomization patients must complete a 14 day period of documented, stable, acceptable standard of care under the care of the principal investigator and must demonstrate an average Visual Analogue Scale (VAS) score of <math>\geq 4</math> (Range 0 - 10), calculated from two VAS evaluations during the last week of the 14 day lead-in phase. No VAS evaluation can be less than 3 and the two evaluations cannot be different by more than three to be considered stable and eligible for randomization. Patients will be allowed to take pain medications as needed during the lead-in period and during the study protocol. Patients will also be allowed to use antibiotics during the 14 day lead-in period if deemed clinically necessary by the investigator. Patients will not be allowed into the study while actively using antibiotics but can remain in the study if antibiotics are clinically required later in the course of the trial. A patient who completes the 14 day documented stable standard of care lead-in phase for the index ulcer(s), demonstrates a stable VAS average pain score and who meets all other study inclusion/exclusion criteria will be randomized to receive one of two treatment courses: a) standard of care with MIST Therapy or, b) standard of care with a sham control. All patients will receive three treatments per week for 4 weeks. Patients must receive 9 of the total 12 treatments and cannot miss more than two consecutive treatments to be considered evaluable. Investigators will be allowed to use their own standard dressings as appropriate for the moisture balance of the ulcer but these will only include standard hydrocolloid, hydrogel, alginate or foam dressings. Changes from one type of dressing to another (e.g. alginate to hydrocolloid) will be allowed as deemed necessary for moisture balance. No advanced or impregnated dressings will be allowed during the study. No topical antibiotics or antibiotic dressings (silver, iodine, etc) will be allowed. Following randomization, ulcer assessments, VAS pain scales and adverse event assessment will be conducted at weekly intervals through week 4; analgesic assessment will be performed three times per week on treatment days; Quality of Life (QOL) scales will be conducted at baseline, week 2 and week 4; sharp debridement will be performed only once per week if deemed necessary by the investigator.</p> <p><b>Progress:</b> This protocol was terminated by the study sponsor for business reasons in January 2007. Two subjects were screened at MAMC; one subject screen failed. The other subject signed informed consent and began the two-week pre-screening process, but did not meet all eligibility</p>		

requirements (could not differentiate leg pain from stump pain) and was dropped from the study. Other sites had reported similar difficulty enrolling.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 206071		<b>Status:</b> Completed	
<b>Title:</b> Phase 3, Multicenter, Multi-National, Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Efficacy and Safety of Alfimeprase in Subjects with Acute Peripheral Artery Occlusion (NAPA-3)					
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD					
<b>Department:</b> Surgery/Vascular Surgery				<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Benjamin W. Starnes, MC; MAJ Kelly S. Blair, MC; Leslie B. Schoneman, PA-C; LTC John D. Statler, MC; MAJ Joseph A. Ronsivalle, MC					
<b>Start - Completion:</b> 7 Jun 2006 - May 2007		<b>Funding:</b> Nuvelo Inc. via The Geneva Foundation		<b>Periodic Review:</b> 8 Mar 2007	
<b>Study Objective:</b> To evaluate the efficacy of alfimeprase compared with placebo as measured by 30 day open vascular surgery free rate. To evaluate: rate of arterial flow restoration at 4 hours after initiation of study drug, rate of improvement in index limb ankle-brachial index (ABI) by 0.15 at 30 days, change in Walking Impairment Questionnaire functional status scores from baseline at 30 days and safety.					
<b>Technical Approach:</b> This is a Phase 3, multicenter, multi-national, randomized, double-blind, placebo-controlled trial with the goal of randomizing 300 subjects. Eligible subjects will be randomized in a 1:1 ratio to receive either intra-thrombus alfimeprase 0.3 mg/kg total dose or intra-thrombus placebo. Study drug will be administered as split doses with 2/3 of the total dose given as the first infusion followed in 2 hours by the remaining 1/3 of the total dose as a second infusion. Both infusions will be given as 1 mL/min pulsed boluses. Subjects will receive both infusions unless otherwise indicated. Study drug will be infused and subjects will be clinically monitored and assessed by follow-up arteriogram 4 hours after initiation of the first dose of study drug. Subjects with restoration of arterial blood flow on the 4-hour follow-up arteriogram will receive no further intervention, endovascular therapy for underlying atherosclerotic lesions or open vascular surgery. The decision to proceed to a particular intervention should be based on functional, symptomatic, and/or physical examination criteria along with locally interpreted arteriographic findings. Subjects without restoration of arterial blood flow seen on the 4-hour follow-up arteriogram will only be eligible for open vascular surgery (e.g., thromboembolectomy). Investigators will be instructed to follow the Acute PAO Management Algorithm (Section 3.4.2) that was modified from the recommendations for the Ideal Management Algorithm for the Treatment of Acute Limb Ischemia Due to Acute PAO. Thirty (30) day open vascular surgery free rate will be the primary endpoint. Restoration of arterial flow rate, increase in ABI by 0.15 rate, change in Walking Impairment Questionnaire (WIQ) functional status scores, and safety will be the secondary endpoints. Restoration of arterial flow will be assessed by the investigator and by a blinded, central Arteriogram Review Committee. Length of hospital stay and length of intensive care unit (ICU) stay up to 30 days as well as WIQ scores and increase in ABI by 0.15 rate at 90 and 180 days after study drug infusion will be exploratory efficacy endpoints. Safety will be assessed by monitoring of AEs, SAEs, major bleeding events, ICH, and peripheral arterial embolic events up to 30 days as well as all cause mortality, AEs, surgical and endovascular procedures and amputation at 30, 90, and 180 days.					
<b>Progress:</b> This protocol received final approval on 7 June 2006; however, the protocol was closed out by the study sponsor 23 July 2007, with no MAMC subjects enrolled.					

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206094	<b>Status:</b> Completed
<b>Title:</b> A Multi-Center, Double-Blind, Randomized, Parallel, Vehicle-and Standard Care-Controlled, Dose-Ranging Study Assessing the Safety and Efficacy of MRE0094 Gel When Applied Topically for 90 Days to Subjects with Diabetic, Neuropathic, Foot Ulcers		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Monica H. Schweinberger, DPM; LTC Benjamin W. Starnes, MC; Mary Anne Landowski, MSN, RN; Thomas S. Roukis, DPM		
<b>Start - Completion:</b> 3 Aug 2006 - Dec 2006	<b>Funding:</b> King Pharmaceuticals Research and Development, INC via The Geneva Foundation	<b>Periodic Review:</b> 22 May 2007

**Study Objective:** To assess the efficacy of 3 concentrations of MRE0094 gel compared to vehicle gel and standard care on complete healing of chronic, diabetic, neuropathic, foot ulcers when applied topically for up to 90 days.

**Technical Approach:** This is a multi-center, double-blind, randomized, parallel, vehicle-controlled, and standard care-controlled dose-ranging study of topically applied MRE0094 in diabetic subjects with chronic, neuropathic foot ulcers. Three concentrations of MRE0094 gel (5 g/g, 50 g/g, and 500 g/g), a vehicle control gel, and a standard care arm using a hydrogel-based product to provide a moist wound environment will be evaluated in a parallel design. About 300 subjects will be randomized in a 1:1:1:1:1 allocation into 5 parallel treatment arms (~60 subjects per treatment arm) to obtain 290 evaluable subjects. Treatment arms will be MRE0094 gel 5 g/g, 50 g/g, and 500 g/g, vehicle gel, and hydrogel (as part of the standard care only arm). Randomization will be stratified based on baseline wound size.

Each subject will complete a 14-day Screening/Standard Care Run-in (SSCR) Period, a Treatment Period of up to 90 days, and a 28-day Posttreatment Period. Subjects who successfully complete all SSCR Period assessments, and who meet all entry criteria will enter the Treatment Period and be randomized to 1 of 3 concentrations of MRE0094 gel, vehicle gel, or hydrogel (as part of the standard care only arm) using a central randomization procedure. MRE0094 gel, vehicle gel, or hydrogel will be applied once daily to the target ulcer for up to 90 days. All wounds will be covered with a saline-moistened gauze pad following each application of study drug. The dressing will be held in place by wrapping it with rolled gauze, and taping gauze to gauze. All subjects will be given comprehensive standard care for diabetic, neuropathic, foot ulcers during the entire study that will include: (1) off-loading the target ulcer using an unaltered Bledsoe Diabetic Conformer Boot plus crutches or wheel chair as needed; NOTE: subjects with Charcot's deformity may use their Charcot Restraint Orthotic Walker in place of the Bledsoe boot, (2) maintaining a moist wound environment; (3) reminding subjects of the importance of proper nutrition and adherence to glycemic control measures instituted by their health care providers; (4) additional sharp debridement if needed; and (5) infection control measures. Following the Treatment Period, subjects will enter the Posttreatment Period. All subjects (with healed or non-healed ulcers) will continue to be given standard care for their target ulcer as described above. Only subjects with non-healed ulcers will apply hydrogel during the Posttreatment Period. Each subject will complete up to 12 clinic visits over the course of the study during which procedures and assessments of safety, efficacy, and protocol compliance will be performed.

**Progress:** This protocol closed on 28 August 2007, with no subjects enrolled. Numerous subjects were screened, but the size of the plantar wound was the biggest factor in the lack of enrollment.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207105	<b>Status:</b> Ongoing
<b>Title:</b> A Prospective, Multi-Centre, Double Blind Randomized Placebo Controlled Clinical Trial To Evaluate The Safety And Efficacy Of ICXP007 In A Phase III Trial With Four-Layer Therapeutic Compression, For The treatment Of Non-Infected Skin Leg Ulcers, Due To Venous-Insufficiency (02-VLU-003)		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Mary Anne Landowski, MSN, RN; MAJ Niten N. Singh, MC; Thomas S. Roukis, DPM; Monica H. Schweinberger, DPM; MAJ Reagan W. Quan, MC; LTC Thomas K. Curry, MC		
<b>Start - Completion:</b> 17 Aug 2007 - Dec 2007	<b>Funding:</b> Intercytex, Ltd via The Geneva Foundation	<b>Periodic Review:</b> N/A
<b>Study Objective:</b> The objective of this protocol is to evaluate the safety and efficacy of ICXP007 in achieving 100% closure of non- infected skin ulcers of greater than three months duration due to venous-insufficiency, with standard four-layer bandage compression therapy.		
<b>Technical Approach:</b> Up to 216 subjects meeting the inclusion and exclusion criteria who have successfully completed the allocated run-in period will be enrolled into the study. Consented subjects, as applicable, will enter a run-in/screening period of four-layer compression bandaging alone. For those subjects where four-layer compression bandaging has been documented as conventional therapy for at least two weeks immediately preceding study consideration, this run-in period may be reduced to two weeks. All other subjects will enter a 4week run-in period.		
If the wound does not heal by greater than 30% (from the first measurement taking at screening) in the allocated run-in period, the subject shall then be randomized into either the Control Group (four-layer bandage compression therapy) or the Treatment Groups (ICXP007 or Placebo treatment and four-layer bandage compression therapy). On the first study/treatment visit (Day 0), subjects in the Control Group will be treated with a non-adherent primary dressing, followed by standardized four-layer bandage compression bandaging. Subjects in the Treatment Groups will have either ICXP007 or Placebo applied to the prepared target wound bed in line with their randomization. Following the application of ICXP007 or Placebo, these subjects will also be treated with a non-adherent primary dressing (see appendix VI) and four-layer compression bandaging (as described in the Study Procedures Manual (SPM)).		
Each subject in the Treatment Groups will be treated by ICXP007 or Placebo over the course of the study. At each follow-up visit, up to and including the study visit at week 20, subjects in the Treatment Group with less than 30% healing from the previous study visit, may be re-treated with ICXP007 or Placebo. Subjects may be treated with up to a maximum of 8 units of ICXP007/Placebo in total. If the subject has received 8 treatments they should not receive any further applications.		
Both the subjects in the Control Group as well as the Treatment Groups will be assessed for the primary study endpoint 1 week following the initial study/treatment visit, and again at 2, 4, 6, 8, 10 and 12 weeks. For secondary endpoints and safety assessment further evaluations will be made at 16, 20 and 24 weeks post-initial treatment..		
<b>Progress:</b> This greater than minimal risk protocol received initial IRB approval on 26 June 2007, and final approval on 17 August 2007. Protocol documents were released to the study staff following CRADA/SOW approval, 10 September 2007.		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206111	<b>Status:</b> Completed
<b>Title:</b> Pivotal Study to Evaluate the Efficacy and Safety of Dermal - Living Skin Replacement (Dermal - LSR) in the Treatment of Chronic Diabetic Foot Ulcers		
<b>Principal Investigator:</b> Thomas S. Roukis, DPM		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD; Monica H. Schweinberger, DPM; Mary Anne Landowski, MSN, RN		
<b>Start - Completion:</b> 18 Oct 2006 - Feb 2007	<b>Funding:</b> ApoPharma Inc. via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The primary effectiveness objective is to determine the efficacy of Dermal -LSR plus Standard of Care (SOC) for the treatment of chronic diabetic foot ulcers (DFUs) in comparison to treatment with SOC alone. The primary safety objective is to determine the safety of Dermal - LSR plus SOC for the treatment of chronic DFUs in comparison to treatment with SOC alone.

**Technical Approach:** This study will be a pivotal, prospective, randomized, controlled, open-label, multi-center study that will evaluate the effectiveness and safety of topically applied Dermal - LSR in chronic diabetic foot ulcers. The study has an open-label design, with the Investigator and the subject being aware of the treatment group to which a subject is assigned. Subjects will be randomized equally to two groups and receive either four topical applications (one per week for up to 4 weeks) of Dermal - LSR in addition to standard of care or will receive standard of care only. There will be a 2-week screening period. Following the consent process and randomization, subjects will be treated according to assignment. Subjects assigned to Dermal - LSR + standard of care will receive one application weekly for up to 4 weeks (or until the ulcer heals, whichever is sooner). All subjects will receive standard of care for the entire study. If the ulcer heals by week 12 or sooner, subjects will be assessed at 1, 4 and 8 weeks post closure. If ulcer does not heal by week 12, subjects will be assessed weekly and will receive standard of care until week 20. If the ulcer heals between weeks 13 and 19, subjects will be assessed one week post closure and at week 20 for the final study visit. Note that if the ulcer heals at week 19, the one week post closure visit and the final study visit will occur together at week 20. Telephone contact will be made 3 days ( $\pm 1$  day) following each treatment visit (for weeks 1 to 4) to assess the well-being of the subjects. Telephone contact will also be made in weeks 5 and 6. The Biostatistics Group from ApoPharma Inc. will generate the randomization scheme.

**Progress:** Approved protocol documents were released to study staff following CRADA/SOW approval 24 October 2006. The PI was notified by the study sponsor that MAMC was being closed as a study site due to lack of subject enrollment on 2 May 2007.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 206127	<b>Status:</b> Ongoing
<b>Title:</b> A phase 2B long-term, randomized, open-label, safety and tolerability trial comparing [S,S]-Reboxetine (PNU-165442G) with routine care in patients with chronic painful diabetic peripheral neuropathy (DPN) Study Number A6061031		
<b>Principal Investigator:</b> Thomas S. Roukis, DPM		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD; Monica H. Schweinberger, DPM		
<b>Start - Completion:</b> 17 Nov 2006 - Aug 2009	<b>Funding:</b> Pfizer via The Geneva Foundation	<b>Periodic Review:</b> 11 Sep 2007

**Study Objective:** Primary objective is to assess the long-term safety and tolerability of [S,S]-RBX in patients with DPN.

Secondary objectives are to assess the effect of long-term treatment with [S,S]-RBX on neuropathic pain and health-related quality of life in patients with DPN and to assess the effect of long-term treatment with [S,S]-RBX on the use of pain-related medications for the management of DPN.

**Technical Approach:** This is a phase 2B long-term, randomized, open-label, safety and tolerability trial comparing [S,S]-RBX with routine care in patients with DPN. Following the screening visit (V1) is a one-week baseline period. At the end of this baseline period (V2), patients meeting the randomization criteria are randomized to either [S,S]-RBX or routine care in a 1:1 ratio. Approximately 800 patients will be randomized at V2. The maximum trial duration is 2 years, during which there will be 14 clinic visits. Thereafter, a final clinic visit (V15) for follow up, will be undertaken, one week after V14. Patients randomized to [S,S]-RBX will be treated with 1mg Q.D. for the first week after V2. At the end of this week they will return for another visit (V3), where the dose may be left at 1mg or, if required for symptomatic reasons, may be increased to 2mg. Thereafter, if required for symptomatic reasons, stepwise dose increase in 1mg increments, up to a maximum total daily dose of 8 mg, will be possible. For reasons of tolerability, the dose may also be reduced in 1mg decrements to a minimum total daily dose of 1mg. Dose adjustment may occur either at a scheduled clinic visit, or at an unscheduled visit. Following dose adjustment, the patient will be contacted by telephone, within one week, to assess tolerability of the new dose level.

Patients randomized to routine care will receive treatment optimized for them on an individual basis. The investigator will be free to provide whatever pharmacological (other than reboxetine/Edronax or opioids†) or other treatment considered optimal for management of the patient's pain, taking into consideration any side effects associated with this individualized therapy. A centralized interactive voice response system will be employed to manage randomization and the allocation of trial drug treatment. Subject to IRB/EC approval/favorable opinion, this trial will include an additional research component involving collection of biological samples for de-identified genetic analysis. The Clinical Pharmacogenomics Supplement to this protocol provides a description of this additional research. Subjects may participate in this trial even if they choose not to participate in the pharmacogenomics component.

**Progress:** Approved protocol documents were released to the study staff in June 2007, following CRADA/SOW approval and IRB approval of Amendment #1. The study remains open to enrollment and continues to screen potential subjects; however, no subjects enrolled during FY07. Nine external adverse event reports were reviewed by the PI and submitted to DCI for the file.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 207022	<b>Status:</b> Ongoing
<b>Title:</b> A Prospective, Randomized, Double-Blind, 2-Part Comparative Study of the Effects of Autologous Platelet-Poor Plasma and Oxidized Regenerated Cellulose on the Healing Rates and Pain Reduction of Split-Thickness Skin Graft Harvest Sites, Combined with the Effects of Autologous Platelet Rich Plasma with Topical Negative Pressure and Topical Negative Pressure Alone on the Healing Rates of Split-Thickness Skin Graft Application Sites			
<b>Principal Investigator:</b> Thomas S. Roukis, DPM			
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD; MAJ Kerry J. Sweet, MC; Monica H. Schweinberger, DPM; Valerie Schade, DPM; CPT Jason T. Perry, MC; Adam S. Landsman, DPM, PhD, FACFAS; Thomas Zgonis, DPM, FACFAS			
<b>Start - Completion:</b> 26 Jan 2007 - Nov 2008		<b>Funding:</b> Exactech Inc. via The Geneva Foundation	<b>Periodic Review:</b> 25 Oct 2007
<b>Study Objective:</b> Autologous Platelet Poor Plasma/Oxidized Regenerated Cellulose Portion Primary: to determine whether a significant difference in the healing rate of split-thickness skin graft harvest sites exists between autologous platelet poor plasma and oxidized regenerated cellulose in patients undergoing limb preservation surgery with the use of split-thickness skin grafts.  Secondary: to determine whether a significant difference in the degree of pain associated with split-thickness skin graft harvest sites exists between autologous platelet poor plasma and oxidized regenerated cellulose in patients undergoing limb preservation surgery with the use of split-thickness skin grafts.  Autologous Platelet Rich Plasma/Negative Pressure Therapy (V.A.C.®) Portion Primary: To determine whether a significant difference in the healing rate of split-thickness skin graft application sites exists between autologous platelet rich plasma with topical negative pressure and topical negative pressure alone in patients undergoing limb preservation surgery with the use of split-thickness skin grafts.			
<b>Technical Approach:</b> Forty consecutive patients, male or female, between the ages of 18 and 80 years, who have adequate vascular supply that would normally be scheduled to undergo a split-thickness skin graft harvest from the ipsilateral thigh with application to the involved foot and/or ankle will be enrolled. Patients will be evenly randomized between the application of autologous platelet poor plasma to the proximal or distal split-thickness skin graft harvest site with oxidized regenerated cellulose applied to the opposite end of the harvest site, as well as, autologous platelet rich plasma with topical negative pressure applied to one-half of the wound being covered with the split-thickness skin graft and topical negative pressure alone applied to the other half. Patients will be monitored during their hospitalization and followed throughout recovery until fully healed at both the split-thickness skin graft harvest site and application site. The time to healing of the split-thickness skin graft harvest site, degree of pain, and complications will be monitored during the above. Photographs of the split-thickness skin graft harvest site will be obtained on each dressing change, as well as, at 12 months post-harvest and evaluated for cosmesis by blinded physicians.			
<b>Progress:</b> This protocol was initially approved by the IRB, 21 November 2006, and received final approval on 26 January 2007. No subjects have been enrolled although screening continues. No changes to the protocol or personnel were reported.			

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207029	<b>Status:</b> Ongoing
<b>Title:</b> A prospective, randomized, single-blind comparison of percutaneous tendo-Achilles lengthening and endoscopic Gastrocnemius recession in diabetic patients undergoing a transmetatarsal amputation with peroneal tendon transfer		
<b>Principal Investigator:</b> Thomas S. Roukis, DPM		
<b>Department:</b> Surgery/Vascular Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD; MAJ Kerry J. Sweet, MC; Monica H. Schweinberger, DPM; Valerie Schade, DPM; CPT Jason T. Perry, MC; Adam S. Landsman, DPM, PhD, FACFAS; Thomas Zgonis, DPM, FACFAS		
<b>Start - Completion:</b> 7 Mar 2007 - Dec 2008	<b>Funding:</b> Geneva via The Geneva Foundation	<b>Periodic Review:</b> 26 Nov 2007
<b>Study Objective:</b> To determine whether a significant difference exists between a percutaneous tendo-Achilles lengthening and an endoscopic Gastrocnemius recession with regard to pedal function (i.e., change in ankle joint dorsiflexion range of motion) and structural alignment (i.e., changes in radiographic alignment measurements) in diabetic patients undergoing a transmetatarsal amputation with peroneal tendon transfers. Secondary: to evaluate the difference between percutaneous tendo-Achilles lengthening and an endoscopic Gastrocnemius recession with regard to risks, complications, expected recovery course, and physiological response during a structured post-operative shoe and custom prosthetic insole program.		
<b>Technical Approach:</b> Thirty consecutive patients, male or female, between the ages of 18 and 80 years, with equinus contracture who have adequate vascular supply that would normally be scheduled to undergo a trans-metatarsal amputation with peroneal tendon transfer will be considered for enrollment in this prospective, randomized, single-blind, comparative study. Patients will be recruited from the Limb Preservation Service, Vascular Surgery Service and Podiatry Surgery Service at the Madigan Army Medical Center who meet the inclusion and exclusion criteria and are willing and able to have informed consent obtained. These patients will be evenly randomized to undergo either a percutaneous tendo-Achilles lengthening or an endoscopic gastrocnemius recession in addition to a transmetatarsal amputation with peroneus brevis to peroneus longus tendon transfer. Patients will be monitored during their hospitalization and followed throughout their recovery until fully healed. The subjective/objective patient scoring systems, skin temperature for each incision site, ankle joint dorsiflexion, computerized gait analysis, and radiographic measurements will be monitored during the above. Demographic differences between treatment groups will be assed using a t-test for continuous data and a chi-square test for nominal data. Plantar pressure variables will be assessed using a 2 (group) x 3 (test occasion) ANOVA with repeated measures. The mean time between tests across all subjects will be used as the interval for repeated measures. Post hoc comparisons will be conducted for variables found to have a significant group-by-test interaction using t-tests with error terms from the ANOVA. An alpha level of 0.05 will be used for all statistical analyses. Statistical analysis will be performed by one of the associate-investigators not involved in data collection or patient identification.		
<b>Progress:</b> This greater than minimal risk protocol was initially approved by the IRB 12 December 2006, and final approval received 7 March 2007. Study remains open to enrollment with no subjects enrolled during FY07, and no changes to the protocol or study personnel reported.		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207082	<b>Status:</b> Ongoing
<b>Title:</b> Bacterial Skin Contamination Prior To and After Surgical Preparation of the Foot, Ankle, and Lower Leg in Patients with Diabetes and Intact Skin versus Patients with Diabetes and Ulceration: A Prospective Controlled Therapeutic Study		
<b>Principal Investigator:</b> Monica H. Schweinberger, DPM		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Thomas S. Roukis, DPM; COL (Ret) Charles A. Andersen, MD; Adam S. Landsman, DPM, PhD, FACFAS		
<b>Start - Completion:</b> 13 Apr 2007 - Dec 2008	<b>Funding:</b> American Academy of Pediatrics via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to determine the type and amount of bacterial pathogens present on the surface of the foot of Diabetic patients, with and without ulceration, and evaluate the effectiveness of a Chlorhexidine gluconate scrub with bristled brush followed by ethyl alcohol with iodine paint in eliminating these bacteria.

**Technical Approach:** Diabetic patients with and without ulcers will be asked to undergo the current "best evidence available" surgical preparation (i.e., chlorhexidine gluconate scrub followed by alcohol impregnated with iodine solution, which has been determined from detailed literature review and a small safety related observational pilot study to be efficacious and safe, respectively). Qualitative aerobic cultures will be obtained prior to and after completion of this surgical preparation technique, from the hallux nail-fold, second, third, and fourth toe web-spaces (as one culture), and anterior tibia (control group). From each culture site the type of bacterial flora present and sensitivity will be determined. Additionally, the reduction in bacterial flora following surgical preparation as described in the materials and methods for both patient groups will be analyzed.

**Progress:** This minimal risk protocol was approved by the Expedited Review Committee on 24 April 2007, and final approval received on 1 August 2007. Protocol documents were released to the study staff on 6 August 2007. No subjects enrolled during FY07.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 07		<b>Number:</b> 206070		<b>Status:</b> Completed	
<b>Title:</b> A Two-Part, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Study to Evaluate the Effect of Simvastatin, Losartan, and Pioglitazone on Cardiovascular Disease Biomarkers in Lower Extremity Atherosclerotic Plaque Excised from Patients with Peripheral Arterial Disease					
<b>Principal Investigator:</b> MAJ Niten N. Singh, MC					
<b>Department:</b> Surgery/Vascular Surgery				<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Benjamin W. Starnes, MC; COL (Ret) Charles A. Andersen, MD; LTC John D. Statler, MC; Leslie B. Schoneman, PA-C; MAJ Andrew S. Bostaph, MC; LTC Ronald R. Magee; CPT Randy J. Kjorstad, MC; CPT Zachary M. Arthurs, MC; MAJ Kelly S. Blair, MC; MAJ Joseph A. Ronsivalle, MC					
<b>Start - Completion:</b> 5 Jun 2006 - Jul 2006		<b>Funding:</b> FoxHollow Technologies, Inc. via The Geneva Foundation		<b>Periodic Review:</b> 27 Mar 2007	
<b>Study Objective:</b> To assess the effect of 6 weeks of treatment with simvastatin, losartan or pioglitazone on the RNA expression profile of atherosclerotic plaque excised from peripheral arteries in the lower extremity of patients with PAD. To assess the effect of 6 weeks of treatment with simvastatin, losartan or pioglitazone on protein and lipid biomarkers in atherosclerotic plaque excised from peripheral arteries in the lower extremity of patients with PAD. To correlate plaque protein and lipid biomarker changes following 6 weeks of treatment with simvastatin, losartan or pioglitazone with changes in circulating plasma and/or serum biomarkers and with blood gene expression profiling.					
<b>Technical Approach:</b> This is multicenter, randomized, double-blind, placebo-controlled, 6-week study, consisting of 3 separate sub-studies in which patients undergoing bilateral lower extremity peripheral artery atherectomy will receive one of three drugs known to have beneficial effect on the risk of cardiovascular disease. Patients will be selected for the particular substudy based on a series of entry criteria and then randomized to the particular agent or placebo for 6 weeks. Following successful completion of a 1 to 2 week placebo run-in period, patients with bilateral symptomatic PAD requiring bilateral revascularization will undergo a unilateral atherectomy using the SilverHawk™ device. The choice of left or right extremity will be determined by random assignment. If treatment of one extremity in advance of the other is indicated either by patient status or physician interest, the investigator will contact the study sponsor to determine whether the patient should be entered. All plaque excised from a given extremity will be collected as part of the study. Based on medical history and concomitant medications, patients will be assigned to one of three treatment groups (simvastatin, losartan, or pioglitazone), and will be randomly allocated to the active drug or matching placebo for a period of 6 weeks. Patients will then undergo repeat peripheral atherectomy on the contralateral leg. A telephone follow-up will be made at Week 8. Blood for gene expression profiling and plasma/serum for circulating biomarkers will be taken at Week 0 and 6. Because of the differential handling of plaque for RNA expression profiling and protein/ lipid measurements, it is not possible to perform both assessments on the same plaque sample. Therefore, the study will be divided into 2 essentially identical parts. In Part A plaque will be evaluated by gene expression profiling. In Part B plaque will be evaluated for protein and lipid biomarkers. An equal number of patients will be enrolled in each Part. After the defined number of patients have been enrolled in Part A for 1 of the 3 study drugs (and its placebo), patients who meet the inclusion and exclusion criteria for that study drug (and its placebo) will then start enrollment in Part B. A total of 336 patients will be enrolled, with a goal of approximately 300 patients completing the study. Each of the treatment groups (simvastatin, losartan, and pioglitazone) will enroll 112 patients, 56 on active drug and 56 on placebo, with the intention of achieving 50 completed patients on active drug and 50 completed patients on placebo. Parts A and					

B will each include 28 patients on active drug and 28 patients on placebo, with the intention of 25 completed patients on active and 25 on placebo.

**Progress:** This greater than minimal risk protocol received final approval 5 June 2006, and study documents were released to investigators following CRADA/SOW approval on 21 June 2006. Two subjects have been enrolled. One subject completed all study related procedures, and one subject screen failed due to lack of disease in both limbs. Amendment #1 changes to the inclusion criteria, and updates of study staff were reported and approved. Several internal adverse events were reported; although none were assessed as serious or unexpected by the PI or Medical Monitor. Subject enrollment continues.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 07	<b>Number:</b> 207010	<b>Status:</b> Ongoing
<b>Title:</b> Plaque Removal versus Open Bypass Surgery For Critical Limb Ischemia		
<b>Principal Investigator:</b> MAJ Niten N. Singh, MC		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Benjamin W. Starnes, MC; COL (Ret) Charles A. Andersen, MD; MAJ Reagan W. Quan, MC; MAJ Andrew S. Bostaph, MC; LTC Thomas K. Curry, MC; Leslie B. Schoneman, PA-C; Monica H. Schweinberger, DPM; Thomas S. Roukis, DPM; CPT Jason T. Perry, MC; LTC John D. Statler, MC; LTC Ronald R. Magee		
<b>Start - Completion:</b> 26 Jan 2007 - Jun 2007	<b>Funding:</b> FoxHollow Technologies, Inc. via The Geneva Foundation	<b>Periodic Review:</b> 4 Oct 2007

**Study Objective:** The primary endpoint is major amputation-free survival (interim analysis will be performed at 6, 12, 24, 36 and 60 months). Secondary Endpoints are (1) 30 day morbidity and mortality, (2) all cause mortality, (3) evaluation of clinical improvement by objective Rutherford-Becker, DUS, Ankle/Toe pressures and QOL assessments, (4) 6 month, 12 month, 24 month, 36 month and 5 year clinical patency and graft occlusion rates, (5) lesion success: 50% stenosis of target lesion(s) at completion of SH procedure or patent bypass graft following surgery, (6) procedural success: no complications and 50% stenosis of target lesion(s) or a patent bypass graft, (7) cost-effectiveness, including length of hospital stay, (8) re-intervention (target lesion(s) and non target lesion(s) evaluated separately), (9) wound Healing, (10) major amputation rate, and (11) minor amputation rate.

**Technical Approach:** This is a prospective, multi-center, randomized controlled study enrolling 400 patients with critical limb ischemia (Rutherford Becker 4, 5, or 6). Patients who meet treatment criteria will be randomized to treatment with the SilverHawk Plaque Excision System or Bypass Grafting. The type of graft and technique utilized during the bypass procedure will be left to the discretion of the operating physician. The plaque material removed during the plaque excision procedure will be collected, shipped to the Sponsor, and profiled using gene and / or protein platforms. No genetic testing will be performed and no cell lines will be established from this material. Blood will be drawn during the index procedure and the specimens will be collected and shipped to the sponsor for potential correlation with tissue findings and patient outcomes.

Patients will be assessed for clinical and functional improvements as a result of their index procedure. The clinical evaluation will include objective Rutherford-Becker classification, ankle/toe pressures, Wagner Classification, wound healing assessment by photography, and arterial duplex ultrasound evaluation. These evaluations will take place at baseline, immediately post procedure, and at 1, 6, 12, 24, 36 and 60 month follow up visits. Functional improvement will be measured using quality of life survey (VascuQOL40) evaluation. These evaluations will also occur at baseline, immediately post-procedure and at 1, 6, 12, 24, 36 and 60 month follow-up time points.

**Progress:** This greater than minimal risks study received initial IRB approval on 24 October 2006, and final approval was received 26 January 2007. Protocol documents were released to the study staff following approval of the CRADA/SOW on 12 February 2007. No subjects enrolled during FY07. Chart screening continues to identify eligible study subjects.

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